®

Supplement to

The Art of Getting Well

Universal Oral Vaccine- With Patents

(Also see Universal Oral Vaccine -- Published Version)

Sources are given in references.

Authors of contributions\quotations are alphabetically arranged; major author, if any, is underlined.

Former Congressman Berkley Bedell (Iowa), Jacob Blumenthal, M.D., Dr. Willy Burgdorfer, Prof. Berry Campbell, Robert A. Collins, Arthur E. Dracy, P. Ehrlich, Fleming, H. Hugh Fudenberg, M.D., Senator Tom Harkin (Iowa), E. Holeckova, August Holm, Charles A. Janeway, Jr., M.D., Calvin Johnson, Attorney, Robert Meade, Dr. Jeffrey Laurence, Lawrence, J.F.A.P. Miller, Dr. Mitchell, D.V.M., Ph.D., Dr. Robert Neurath, Gary V. Paddock, Prof. William E. Peterson, Peng Giancarlo Pizza, Ph.D., R.M. Porter, Ph.D., Dr. Paul K. Pybus, Herb Saunders, B. Sekla, Clarence Siegel, M.S., Cyril M. Smith, M.D., Herbert Struss, Ph.D., Caterina De Vinic, C.J. Watson, M.D., Philip F. Weighner, Gregory B. Wilson, Michael Zasloff/Responsible editor/writer Anthony di Fabio.

The Roger Wyburn-Mason and Jack M. Blount Foundation for the Eradication of Rheumatoid Disease

AKA The Arthritis Trust of America®,

7376 Walker Road, Fairview, TN 37062

Dream Cure!!

As doctor or patient, how would you like to have a combined allergen and antigen vaccine that is:

- 100% safe for 100% of those who use it;
- can be taken orally in small doses without any distaste;
- can be manufactured in virtually every country in the world with the technology available to each country;
- is cheap, so cheap, that virtually everyone in the world can easily afford it;
- is ubiquitous, in that it will protect against any organism (including virus, rickettsia, parasite, protozoan, bacteria, mycoplasm, yeast/fungus, amoeba) or any allergen (including exogenous and endogenous sources), and might, just might, also dry up to blow away a number of cancers?

What would such a dream cure do for the pharmaceutical industry?

Dry it up so it would also blow away?

Brief Background on Immune Milk

The subject of immune milk has played a prominent -- if not pivotal -- role in understanding antibodies and immune reactions.

According to former University of Minnesota professors, Berry Campbell and William E. Peterson,[20] since P. Ehrlich's first investigations in 1892, and his definitive "magnum opus," our understanding of immune functions and the importance of the transfer of immunity from one species to another was mystified thereafter by a rash of poorly performed research, clouded conclusions, and consequent loss of interest for a period of many years.

The nature of both passive and active immunity has been defined with some certainty in one era, only to be redefined with equal certainty in another. Despite all of the confusion and inadequate research taken to be gospel, Ehrlich's work stood the test of time, as did key research papers written by a tiny handful after Ehrlich.

What follows will demonstrate what many of us had wrongly held to be true -- that immune transfering agents which create passive immunity cannot be extended into what appears to be a (long-term) form of active immunity.

Colostrum (first milk) was finally determined to be exceedingly important for most mammalian species, including man. Campbell, Porter and Peterson[20] (1950) examined the udders of cows during parturition, determining at last exactly where immunity protective elements were manufactured in large numbers.

"The importance of these cells was again stressed in the Ph.D. thesis offered (1951) by R.M. Porter, whose experiments included the injection of killed bacterial vaccines into the teat canal of the cow and the demonstration of the early return of specific antibody."[20] (In addition to anti-bodies, milk cows so treated will also pass into their milk T cells -- about 1/2 by ratio of other protective substances -- interleukin 2, gamma interferon, macrophages, and so forth.)

Campbell and Peterson hypothesized that the chief evolutionary advantage for the mammalian suckling is not so much nourishment gained, but rather to provide the opportunity to pass allergens or antigens directly from the environment surrounding the newborn into the teat of its mother, whence specialized cells manufacture in great quantity necessary protective antibodies that are subsequently passed back to the suckling. On receiving the protective colostrum, the suckling's immature gut (leaky gut) absorbs the protective elements directly into the blood stream, and is thus protected.[20]

While many antigens may pass directly from the environment through the teat, the dominant feature would be the act of transmission during nursing -- the calf would itself pass along micro-organisms which would be the same, of course, as those to be protected from. This is called "diathelic immunization."[20]

Two basic facts stand out, according to Petersen: (1) The mammary gland will respond with antibody production to most antigens properly infused therein; and (2) When enough of such milk is consumed at a time, the antibody will be absorbed from the gastrointestinal tract into the blood.[21]

Homeopathy Squared

In the patents that follow as detailed, supporting documents, an antigen or allergen is introduced into the cistern (base of teat) of a cow and the resulting milk produces a substance that can be used as a homeopathic "mother."

Those who practice homeopathy know that when creating a series of dilutions from a "mother" -- i.e., the initial fluid that contains the dead antigenic materials or allergens -- that the first dilution with sterile water is 1 (volume of the mother) to 9 (volumes of sterile water), the second 1 to 99, the third 1 to 999, fourth 1 to 9,999, fifth 1 to 99,999, sixth 1 to 999,999, etc., called, respectively, 1X, 2X, 3X, 4X, 5X, 6X, and so on. Each successive ratio is percussed, shaken or tapped, to store whatever active biological message is contained in the original mother.

When used in medical treatments, the mother containing the (deadened) antigen or allergen is diluted according to the above ratios often to the point where -- according to known scientific principles -- the probability, P, of finding a single molecule of the original antigen or allergen from the mother in the higher potencies is so close to zero that for all practical purposes it is zero. [P - 0 = e; e approaches 0 as dilution increases, where e is a vanishingly

small quantity.]

Contrary to all apparently rational reasoning, as practicing homeopaths report, the greater the dilution, the stronger the effects on the patient.

In the universal vaccine to be described, the mother is derived from a milk or milk product (whey, colostrum, or milk) that can be used effectively raw, pasteurized, pasteurized and lypholized, or can be made into a homeopathic substance.

In the patents that follow, in scientific studies on the degree of protection for mice that have been infected with known pathogens, mice survived much better at the 6X potency than at the 3X potency. The 1 to 999,999 dilution was a better protection than the 1 to 999 dilution and, of course, pure water (control group) without any relationship whatsoever to the mother resulted in very high fatalities. This result is consistent with claimed homeopathic principles.

What is new to homeopathy -- from the little I've read -- is this: The mother prepared for the first cow has virtually no potential of containing a deadly (alive) antigen or allergen, but can be injected into the (cistern) of the cow, thus producing from that cow a second mother. When this second mother is diluted to 1 to 999,999, or 6X, it has the same protective capacity as the studies demonstrated from the first mother!

Even more perplexing is the fact that when the 6X dosage is cut by 1/2 or 1/4, protection of mice from introduced pathogens is increased!

Complement Activity

Complement is an enzyme substance which produces disintegration of bacteria or blood cells.

Obviously antigen/antibody complexes are involved in protection from antigens or allergens, but the scientist who has spent the last 20 years isolating out the active ingredient in "immune" milk -- and prefers not to be identified -- feels that C3B (anti-complement) weighing about 1200 daltons is the active ingredient.

When the body signals white cells to swarm to a local area for the purpose of killing invading organisms and to begin the healing process, an over-reaction creates pain and inflammation. Anti-complement, C3B, dampens the over-reaction. Normal milk does not contain anti-complement, whereas cow's milk from cows that have been treated through the teat into the cistern with antigens or allergens contains a relatively large quantity of anti-complement.

Complement activity, generally, can be triggered in 3 different ways, according to Charles A. Janeway, Jr., M.D.,[1] professor of immunobiology and biology at Yale University.

• C3 can bind to any protein, such as bacteria. Cells from one's own tissue are protected by proteins that inactivate C3. Once bound to the microbe the C3 molecule causes other complement molecules to bind to the bacterium. This cascade of complement, and their functions, destroys the bacteria.

• A macrophage secretes interleukin-6 after detecting an infection. The interleukin-6 is carried through the bloodstream until it reaches the liver where it causes the liver to secrete mannose-binding protein. Mannose-binding protein binds to the bacterium capsule and triggers the complement cascade, thus destroying the bacterium.

• B cells become active if they bind to a bacterium, and are stimulated by so-called helper T cells. The B cell proliferates and secretes antibodies. The antibodies bind to bacterium which also activates a complement protein known as C1q, which also activates other complement molecules, thus destroying the bacterium.

• Complement can also recruit other immune system cells, such as phagocytes.

• Molecular biologist Michael Zasloff (president of Magainin Research Institute) and colleagues detected a microbe-killing peptide on cow's tongues. When slight wounds resulting from grazing were found on cow's tongues, cells on the surface of the tongue began increasing the amount of bacteria-protective peptides. They found that the peptide is produced on every other wet surface of the cow's body -- eyes, lining of gut, and airway. Similar antibiotic peptides were found in the gut and airway of humans as well as in the skin of frogs and the stomach of sharks. "The amazing thing," Michael Zasloff says, is that in some places like the tongue, which are exposed to a continual assault, you always have a low level of expression, so there's a barrier all the time. But when you're injured, the barrier doesn't get weak -- it gets stronger."[32]

• According to Fudenberg and Pizza, Dialyzable Leukocyte Extract contains immunologically active peptides that boost the recipient's own cell-mediated immunity in an antigen-specific manner. These moieties (which may or may not be related to cow's peptides) have a molecular weight approximately 1500 to 2000 daltons.[25] ("Immune System Protection from Foreign Invaders," http://www.arthritistrust.org.)

Transfer Factor Activity

Transfer factor -- apparently an older medical term -- is a family of communication molecules that can stimulate or transfer cell-mediated immunity against certain diseases in man and other animals; and also transfer factor can be made, or passed, between species.[18]

"Lawrence demonstrated that delayed cutaneous hypersensitivity responsiveness could . . . be transferred by soluble extracts of leukocytes from 20 ml of blood and termed the factor responsible for this phenomenon 'transfer factor'. Transfer factor could transfer delayed cutaneous hypersensitivity of a given specificity from a skin test positive individual to a normal skin test negative individual, hereafter termed primary recipient. Within six months, white cells obtained from this primary recipient could be similarly fed and the leukocyte extract given to a secondary recipient negative by skin test. This secondary recipient, too, would become positive in accordance with the specificities of the first donor."[26]

• "In 1962 J.[F.A.P.] Miller showed that the immune system in chickens could be divided into two components, namely, the B-lymphocyte, derived from the bursal system (B cell), producing antibodies that protect against infection from classic micro-organisms (pneumococcus, meningococcus, streptococcus, gonococcus, etc.) and thymic-dependent (T cell) systems that protect against fungi, parasites, viruses, mycobacteria, and cancer metastases."[25] Both colostrum and milk contain antibodies including T cells, B cells and macrophages.[18]

• According to Fudenberg and Pizza, "We now know that the extract obtained by the Lawrence method contains at least 200 different moieties with M[olecular] W[eight] from 1 to 20 kilodaltons and that only one of them is antigen-specific T[ransfer] F[actor] with a M[olecular] W[eight] of approximately 3.5 to 6 kilodaltons."[25,26] The ratios and quantities of the various antibodies and cell types vary between milk and colostrum for a given species and between species.[18] ("Substitution of the anti-coagulant EDTA-sodium to obtain blood from other species has now made it possible to obtain dialyzable leukocyte extract from a host of non-human species (*vide infra*), according to Fudenberg and Pizza).[25]

• Although antibodies produced in colostrum can survive an infant's digestive tract and confer immunity at least in some species, the various cell types found are less hardy, and, if they do survive are believed to provide immunity only to localized regions, although, according to present belief, "cell-mediated immune phenomena might be transferred from mother to young from passage of soluble factors produced by lymphocytes, such as transfer fac-

tor."[18]

• Fudenberg and Pizza now reserve the termT[ransfer] F[actor] for the components of the dialyzable leukocyte extract (DLE) that transfers T-lymphocyte responses in an antigen-specific fashion; that is $TF_{a.s.}$. "This fraction, in turn, contains a multitude of T[ransfer] F[actor]s corresponding to the sum of immune experiences of the individual subject."[27]

• Characteristics[25] of transfer factor include the following: 3,500 to 6,000 daltons in size; heat labile but cold stable (-20^0 to -70^0 C storage for several years); RNA bases attached to small peptides, oligoribonucleotide-peptide complexed in vivo; breaking bonds destroys biologic activity; contains at least eight amino acids, therefore possible to have several billion variations in primary structure; as 28 of the 20 known amino acids have been found in various semi-purified transfer factors, the number of variations in primary structure (combinations) may be 8^{18}; a mixture of several moieties is preferable since nature designed in the immune system molecules that work synergistically when combined (mixture of gamma-interferon, with "contaminants," benefited 50% of patients with a wide variety of cancers, but when freed of "contaminants" produced 1% clinical benefits in pure form.)

• Dialyzable Leucocyte Extract may be administered by subcutaneous, intramuscular injection, intravenous, oral administration, by suppository, or incorporated into liposomes so that the biological activity persists for a longer duration, and is remarkably free of seirous side effects.[25]

• There is a blocking agent in colostrum or milk inhibiting cell mediated immunity, as demonstrated in vitro, but the discovery of the presence of large quantities of transfer factor in colostrum is totally unexpected, leading to the development of readily available, inexpensive sources of this otherwise rare and expensive substance.[18]

• Serum and blood do not contain transfer factors unless the lymphocytes have been stimulated by an antigen.[18]

• To serve as a useful transfer factor, helper T cells ought to markedly outnumber suppressor T cells (as in peripheral blood) since suppressor cells are a source of products believed to negate the effects or action of transfer factor.[18]

• The relative ratios of helper and suppressor T lymphocytes are lower in colostrum than in peripheral blood.[18]

• Although desirable protective transfer factors can be obtained from the tissues of blood serum leukocytes or lymph node lymphocytes, these sources require costly extraction processes, often require the sacrifice of animals, and are of very low yield.[18]

• Transfer factors are specific for a given antigen to which the source animal has received prior exposure or immunization; and that antigen specificity can be obtained when leukocytes are incubated with that antigen or organism from which that antigen is derived.[18]

• Transfer factor for a given antigen can be induced by serial transfer of transfer factor for that antigen from an immune subject to another subject -- and from one species to another species.[18]

Bright -- For Me! -- Conclusions

When vaccination is used, large quantities of antigens or allergens are introduced into the human body. The object is to bypass normal immunological defenses, and to induce the body to produce vast quantities of antibodies which, presumably, result in (memory cell) protection against antigens or allergens.

• Since virtually vanishing quantities of protein molecules (C3B) or transfer factors in homeopathic remedies bring about vast, certain protection, large quantities of antigens or antibodies are unnecessary, possibly somewhat dangerous in some cases, and possibly overburden the body with unnecessary stress.

• If the end object of vaccination with the use of antigens and allergens is to bring about production of complement and protective transfer factor, when under attack, then why not introduce the complement and transfer factor directly, as seems to work under the studies performed in the patents (# 3,376,198; 4,816,563) to be described in the following?

• Apparently the homeopathic "communication" of the correct complement -- through the sterile water vehicle (Patent #s 4,402,938; 4,843,065; 5.102,669) -- is the ultimate essence for necessary protection, but in a different manner consumption of transfer factor found in properly prepared colostrum can also play a leading protective and curative role (Patent # 4,816,563).

Result of Berkley Bedell's Cure

As you may know, Iowa Senator Tom Harkin, and others such as former Iowa Congressman Berkley Bedell, pushed through the new Office of Alternative Medicine under the National Institute of Health. Such a political move in the face of hostile pharmaceutical agents had to have a lively unseen foundation.

When former Congressman Berkley Bedell from Spirit Lake, Iowa testified before the Senate Health Appropriations Subcommittee chaired by Senator Tom Harkin on June 24, 1993, my research/development interest was peaked.

Berkley Bedell had suffered from Lyme Arthritis Disease which is caused by the bacteria *Borrelia burgdorferi* derived from ticks. He was cured by a few teaspoons of specially prepared cow's whey.

While I have yet to trace everything to its bitter roots, factors which puzzled were this:

• How could a teaspoon of cow's whey taken every 1-1/2 hours for a few weeks possibly cure Berkley Bedell's long-standing Lyme Arthritis Disease?

• According to the patent, the protective product and supportive material can be developed to treat any kind of allergen and any kind of antigen from microbial agents: bacterial, viral, protozoal, rickettsial, mycoplasmic, yeast/fungal. (Yes, even candidiasis.) The product can be developed to mix the various allergens/antigens together. (See "Candidiasis: Scourge of Arthritics," http://www.arthritistrust.org.)

• Since April 2, 1968, a patent has existed describing in detail how to prepare this oral vaccine, and the patent has been added to over the years.

• When testing the beneficial claims of alternative medical procedures, if one wishes to denounce the claims, a common practice includes altering the nature of the study; that is, change the dosages, modify the study parameters, substitute an improper chemical or study population, and then announce to the world that the original claim was proven to be untrue. Apparently the Department of Agriculture was also not beyond such tactics. In a court trial, too many irregularities (almost total disregard for scientific duplication of experimental design) were displayed in a study conducted by the U.S. Department of Agriculture presuming to duplicate the results of the patent ["Method of Producing Antibodies in Milk," (Patent # 3,376,198)].[34]

Impro Products Co., Inc., a small Iowa company, fought the long battle to expose U.S. Department of Agriculture (Animal Research Service, Beltsville, Maryland, 1966-67) "incompetence," and won in the U.S. District Court of Columbia where the court declared that the U.S. Department of Agriculture report (*American Journal of Veterinary Research*) "contained false and misleading information and that by releasing it the USDA displayed arbitrary and capricious action and an abuse of discretion." The judge enjoined the USDA from further releasing the report.[34] Impro Products Co., Inc. was at last vindicated, with attorney fees paid, but, after 14 years of battle, the war was far from over.

With the assistance of Congressman Rose from the dairy subcommittee, and other Iowa senators and congressmen, Impro Products Co., Inc. was able to get legislative approval, and presidential signature, for extension of the patent rights an additional 15 years. Only four other patents had been extended in the prior 30 years, and each of these were large industries well represented in Washington, D.C., one being for the United Daughters of the Confederacy, protecting emblems of religious, fraternal, and patriotic organizations. Other patent extensions included G.D. Searle Co. for Aspartame because FDA caused an unusual lengthy delay in testing the product; an anesthetic called Forane, and a general class of oral hypoglycemic drugs, these last three extended under the general argument that the patent rights were initially suspended in the interest of public safety.[35]

An early researcher, Herbert Struss, Ph.D., held an Investigate New Drug number (IND) from the FDA in the 1960s. His cooperating physicians were making great gains in using Immune Milk, when the FDA capriciously and arbitrarily closed down the operation, not by canceling the IND, but rather by threatening to place the investigator in jail if s/he did not cease and desist. As the investigator had a family to support, s/he complied, and spectacular early results from the use of Immune Milk was lost to humankind.

What's Going On?

Has a Universal Oral Vaccine been handily suppressed for numerous years?

Congressional Testimony

When former Iowa Congressman Berkley Bedell[2] testified before the U.S. Senate Health Appropriations Subcommittee Chaired by Senator Tom Harkin, also of Iowa, on June 24, 1993, he gave witness to a powerful and obviously safe method of solving Lyme Arthritis Disease, and presumably other diseases.

He described a procedure whereby the killed bacteria, *Borrelia burgdorferi*, was injected above a cow's udder, above the base of the teat (where the antigen or allergen is sure to reach the cistern), prior to the birth of her calf. Colostrum -- the cow's first milk after the calf is born -- is processed into whey -- the liquid left after milk has been coagulated by the aid of a coagulating enzyme called rennet.

Congress Bedell also gave witness to the effects of an overpowerful, suppressive governmental organization that would prevent people from trying (every 1-1/2 hours for a few weeks) the whey of this milk, to learn if their Lyme Arthritis Disease will disappear. He reports that the company that cured him "dares not sell such a medicine, because of FDA regulations."[3]

Discovery and Distribution of Lyme Arthritis Disease

The unlucky invasion of *Borrelia burgdorferi*, the spiral-shaped microbe injected by at least one species of tick, *Ixodes scapularis*, seems to present the unwitting victim with arthritic symptoms that also may require more than one approach for its solution.

There are about 1,200 cases of Lyme Arthritis Disease (also called Lyme Disease) reported across the United States each year (1,282 reported in 1993)[4]. The disease remains concentrated along the coastal plain of the Northeast and mid-Atlantic region, in the upper Midwest, and along the Pacific coast, although the disease has been reported in 32 states.

In a *Science News* report, researchers at the University of Connecticut Health Center in Farmington and the Yale-New Haven Hospital examined 70 children diagnosed with Lyme Arthritis Disease and found that only 53% actually harbored the Lyme-causing bacterium *Borrelia burgdorferi*. The remaining 47% had been misdiagnosed.[4]

The cause of Lyme Arthritis Disease was determined to be a microbe transmitted by a tick, in this first instance, from the species *Ixodes capularis*. Since this tick was common in the grasses and woods near Lyme, Connecticut, the cluster of symptoms obtained the name "Lyme Arthritis Disease."

As Dr. Willy Burgdorfer, who worked for Rocky Mountain Laboratories in Hamilton, MT, identified the damaging microbe, the bacteria was named *Borrelia burgdorferi*, which is a spiral-shaped bacterium similar in shape to the spirochete, *Treponema pallidum*, which causes syphilis.

Since this initial set of discoveries, it's clear that similar diseases have existed in Australia, Africa, Europe and Asia. It also appears in every one of the states in the United States, but seems to be particularly common in northern California, Minnesota and the northeast.

Infection by *Borrelia burgdorferi* occurs chiefly in the spring, summer or early fall, because of the life cycle of the *Ixodes scapularis* tick. (Also see "Mycoplasma Experiments," http://www.arthritistrust.org.)

The Edited Testimony of Former Congressman Berkley Bedell (Iowa)[2]

"My name is Berkley Bedell. I am the founder of Berkley and Company, a major fishing tackle manufacturing company which I started in high school with $50 saved from my newspaper route. I was the nation's first small business-person of the year, and served in the United States Congress from 1975 until 1987. I fully realize that this background does not qualify me as one of the scientific experts on health. I happen to think that is good. I start with no preconceived beliefs on health care that may need to be changed.

"I serve on the ad hoc advisory committee to [The Department of Health's] new Office of Alternative Medicine. I am knowledgeable about some of the problems it faces in conducting the 'investigations and validations' called for in this legislation.

"I left Congress because I came down with Lyme Disease which I contracted while fishing at Quantico Marine Base, and which conventional treatment failed to relieve. After 3 series of heavy antibiotics infused into my veins over a period of 2 years, I finally turned to unconventional treatment. My symptoms disappeared and today I am clearly free of Lyme Disease.

"Let me tell you about that treatment. There is a company in our own state of Iowa, Mr. Chairman, that produces a product for livestock by injecting killed germs into the udder of a cow prior to the time the cow has a calf. When the cow has the calf they then take the first milk that the cow gives, which is called colostrum, and process it into whey so that it will keep.

"The theory is that the cow will communicate the disease to the unborn calf, and will develop the antibodies, or whatever, in the colostrum to protect the newly-born calf from that disease.

"After I took a teaspoon of this whey every 1-1/2 hours for a few weeks, my symptoms of Lyme [Arthritis Disease] disappeared, and I no longer suffer from that disease. Because of the publicity of my case, I get frequent phone calls from desperate people who have been unable to get relief from Lyme [Arthritis Disease] with conventional treatment. It breaks my heart that I cannot tell them about my treatment, because no one has been willing to spend the millions and millions of dollars necessary to get FDA approval to market this special whey. I can tell you it cured what appeared to be arthritis in my knee in 15 minutes."

"I have talked to a doctor in Wisconsin who was using this material. He claims 80-90% success in treating patients like me for whom conventional treatments have not been effective. He has now been advised by the Iowa producer that the material will no longer be available because the producer is afraid of the FDA."

What is Lyme Arthritis Disease?

Lyme Arthritis Disease is a systemic arthritic-like disease caused by a bacteria that is carried by ticks, resulting in characteristic symptoms difficult to diagnose without noting initial symptoms. About 10% of those infected have a very difficult time getting well, and the disease can linger on for years. (See "Lyme Disease: Arthritis by Infection," http://www.arthritistrust.org.)

The Dairy Farmer Who Cured Former Congressman Berkley Bedell

Some years ago a written complaint was sent to Minnesota Attorney General Hubert Humphrey, III, against Herb Saunders, 66, St. James, Minnesota farmer, for selling a woman colostrum. The woman later died of cancer. The victim's husband did not complain, and he was upset that there was a complaint written.[33]

Hubert Humphrey, III, got the FDA into the act, and, after two years of study, decided that Saunders' activity was not in their jurisdiction.[33]

The FDA turned the case over to the Minnesota Bureau of Criminal Apprehension where eventually investigation resulted in a charge of fraud, animal cruelty, swindle and practicing medicine without a license under two subdivisions:

(A) MNSTAT 147.081 Subdivision 3 (2): *Offers or undertakes to prescribe, give, or administer any drug or medicine for the use of another;*

(B) MNSTAT 147.081 Subdivision 3 (3): *Offers or undertakes to prevent or diagnose, correct, or treat in any manner or by any means, methods, devices, or instrumentalities any disease, illness, pain, wound, fracture, infirmity, deformities, or defects of any person.*[33]

Obviously (B) MNSTAT 147.081 Subdivision 3 (3) is overbroad and actually infringes on constitutional guarantees of freedom of speech. Unfortunately, the Minnesota Appeals Court was unable to reach this decision because the premise had never been certified from the lower court.[33]

MNSTAT 147.081 Subdivision 3 (3) was withdrawn as a charge against Herb Saunders after a felony 12 person jury was established and the expert witness list was distributed. With its withdrawal a 6 person jury was reconstituted.[33]

Apparently these preliminary trial preparations brought to the prosecutor's attention that expert witnesses just might make a mockery of some of the absurd charges, and so all that remained against Herb Saunders was (A) MNSTAT 147.081 Subdivision 3 (2), one of the Minnesota statutes intended to inhibit the practice of medicine without a license.[33]

Herb Saunders, the farmer who cured Congressman Bedell, was prosecuted in St. James, Minnesota by the state prosecuting attorney for practicing medicine without a license. Herb was selling bovine colostrum ("first milk") as a potential cure for cancer. "Saunders would sell each patient a cow for $2,500, but keep the cow on his farm. He would inject a sample of each patient's blood into the cow's udder [cistern], and then sell the colostrum to the cow's owner for $35 a bottle. Saunders told an undercover state agent who posed as a cancer patient that he would 'cough out' his cancer within months if he would take colostrum, [and] refrain from chemotherapy.

"After two weeks of [court] trial -- the longest this small community had ever seen -- the result was a hung jury. The 6-person jury voted 5-1 to convict, but the last holdout, a part-time social studies teacher, apparently couldn't decide whether Saunders was practicing medicine without a license or offering an alternative type of care that is not medical practice."[5]

Berkley Bedell provided $21,000 for Saunders' defense.

"The Watonwan County attorney's office stated that it plans to retry Saunders (1996).

"Saunders' attorney, Calvin Johnson, stated that he will try to have the state's medical practice act declared unconstitutional based upon its vagueness, or have the state legislature change the law before Saunders is retried." However, the next scheduled crack at Saunders through a second Grand Jury action began May 17, 1996.

[Reported by attorney Calvin Johnson, Herb Saunders' trial once again resulted in a hung jury, reportedly more hung than the first one. The district attorney dismissed the case on May 30, 1996, and will not retry Saunders.}

Sanders approach seems to be well substantiated by the work of Peng, et. al., Fudenberg, Pizza and others, using dialyzable placental lymphocyte extract.

Background That Applies to the"Universal" Cure

Except for an abandoned patent petition number 628,987, filed October 25, 1945, by August Holm (Merck Chemicals sponsor), the original work on development of cows'-milk vaccine, called "Immune Milk," was performed at the University of Minnesota, School of Biochemistry, under the direction of the patent assignees. (Porter: *Biological Abstracts* 1953, p. 951, par. 10, 185). In August, 1951, Dr. Porter, then "working on his doctoral thesis, suggested the possibility of manufacturing antibodies in the cow's udder by infusion of antigen into the udder of a lactating cow."

The earliest patent seems to be that of patent number 587,849, December 1, 1959 in Canada by William E. Petersen of St. Paul, Minnesota and Berry Campbell of Monrovia, California.

The International Association on Immunity was founded in 1963 by Herbert Struss, Ph.D., William E. Peterson, Ph.D., and Robert Meade. That Association published three issues of *Journal of Immune Milk*. In the first journal Campbell and Peterson summarized "The Current Picture," a resume of the history of knowledge of immunity up through 1961; and that issue, as well as the two following, published patents included here, as well as articles by others. Intent was, according to Dr. Struss,[31] also editor of the *Journal*, to follow up with an issue on Russian research as well as that on viruses by Dr. Mitchell, D.V.M., Ph.D. in Canada.

Dr. Mitchell had performed almost identical work to that of Dr. Peterson but on viruses, especially Newcastle's disease, and, according to Dr. Struss,[31] his work was "just fantastic."

Herbert Struss, Ph.D.[31] published "Immune Milk Treatment of Rheumatoid Arthritis -- Review" June 1964.

Arthur E. Dracy published "Immune Milk in the Treatment of Poison Ivy" June 1965.

Herbert Struss published "A History of the Use of Immune Milk in the Treatment of Fall Pollenosis" in June 1965.

On April 2, 1968, patent number 3,376,198,[6] "Method of Producing Antibodies in Milk," was granted to William E. Petersen, St. Paul, Minnesota and Berry Campbell, Monrovia, California, assigned to Collins Products, Inc., Waukon, Iowa.

Gregory B. Wilson and Gary V. Paddock, both of Mount Pleasant, North Carolina, were granted patent number 4,816,563, "Process for Obtaining Transfer Factor from colostrum, Transfer Factor So Obtained and Use Thereof," March 28, 1989.

Robert A. Collins and Philip F. Weighner of Waukon, Iowa, were granted patent number 4,843,065 June 27, 1989 for "Method of Producing Products for Use in the Treatment of Bacterial and/or Virus Infections."

Robert A. Collins of Waukon, Iowa was granted patent number 5,102,669; April 7, 1992 for "Method of Producing Remedies and Products of the Method."

Giancarlo Pizza, Caterina De Vinic and H. Hugh Fudenberg published "Transfer Factor in Malignancy," *Progress in Drug Research*, Vol. 42, in 1993. This was a joint paper by S. Orsola-Malpighi Hospital, Bologna, Italy, and NeuroImmuno Therpeutics

Research Foundation, Spartanburg, South Carolina.

H. Hugh Fudenberg, Ph.D. and Giancarlo Pizza, Ph.D. have summarized a great deal of their own original research, "Transfer Factor 1993: New Frontiers" in *Progress in Drug Research*, Vol. 42 on behalf of the NeuroImmuno Therapeutics Research Foundation, Spartanburg, South Carolina. Therein it is concluded that bovine colostrum milk is almost the ideal source for obtaining protective factor.

In 1994, H. Hugh Fudenberg, Ph.D. published "Heterogeneity of Alzheimer's Disease: An Interpretive Review, in Molecular Neurobiology" in Human Press, Inc.

Dr. Fudenberg's overall research eventually led to production of antigen-specific immune factors produced by Chisholm Biological Laboratories, PO Box 1289, Aiken, SC 29802; (800) 664-1333.

The overall history of "Immune Milk," should not ignore the tremendous research performed at Stolle Milk Biologics International of Cincinnati, OH, involving Ralph Stolle, Lee Beck, Ph.D., and others. Possibly more related patents were completed by this organization than any other, and they are still active in producing health products developed under their patents through the New Zealand Dairy Board.

What is the Protective Principle?

The protective activity "seems to be a system of peptides that is produced by the cow. . . . Basic research beginning in the late sixties was directed to identify the active products (biological and chemical) in the whey product. This has proven very difficult and especially because the activity is not an antibody per se, but appears to be the action of a low molecular weight material.

"Several important activities can be found in the product that is produced by infusion of specific antigens into the udder (to be placed just above the udder into the cistern) of a cow after collecting the colostrum and milk for the final product production:

• ***Anti-complement Activity:*** The whey exhibits anti-complement activity at the C3B stage, the stage when the body is prevented from calling in the white cells (over-reacting). C3B also aids in antigen phagocytosis.

• ***Anti-Infection Activity:*** Mice injected intraperitoneally (other than oral) with lethal numbers of bacteria or viruses are dead within 12 to 24 hours. Using a whey product containing the antigen specific to the bacteria or virus, that was provided to the challenged animal, will prevent death.

• ***Transfer Factor:*** The whey product also contains transfer factor with specific activity as regards the antigen employed. This is tested in guinea pigs for delayed hypersensitivity.

• ***Titer:*** Whey products demonstrate titer values employed for the antigen used in infusion to be between 1 to 10,000 to 1 to 100,000.

• ***T Cell Stimulator:*** More recently the products which reduce white cell over-activity also increase the number and activity of T cells."

Sources of Protection

Reminiscent of what has become the routine human use of dimethylsulfoxide (DMSO) or antibiotics restricted by law to veterinarians and those practicing animal husbandry, marked "Not For Human Use," some dairy farmers purchase products for their animals' disease protection, but use the products on themselves with success.

Those with access to a cow can purchase standardized antigens (killed) or allergens from biological supply sources which can be innoculated through the cow's udder or into the base of the udder (into the cistern) at the proper time before calving. A variety or blend of organisms or substances -- pollen, cat, dog, or cow hair if one is allergic, or specific antigens against a given disease condition -- will result in a milk product that will cure and protect from an equally large and varied number of pathogenic organisms or allergens, respectively.

There is some evidence that some forms of cancer will succumb. Czechoslovakians B. Sekla and E. Holeckova,[22] reported on the results of tumor implants in rats. Protection was enhanced considerably by the use of immune milk developed from sheep, as opposed to normal milk, or to those rats receiving neither.

Herbert E. Struss, Ph.D.,[23] Director of Research for the W.E. Petersen Research Institute, reported on the effective use of *Staphylococcus aureus, Streptococcus viridins, Streptococcus hemolyticus*, and *Diplococcus pneumoniae* against Rheumatoid Arthritis.

Usually first milk, the colostrum, contains the greater quantity of protection, although any of the milk products can be pasteurized, processed, freeze-dried, and stored for later use, if properly handled.

Limited homeopathic remedies based on the described principles can be obtained from Beaumont Bio-Med [PO Box 6 Waukon, Iowa, 52171]. Health conditions apparently aided based on particular (specific) antigens or allergens introduced into the homeopathic initial solution (mother) are Rheumatism, Rheumatoid Arthritis, coughing, respiratory, sore throat, skin conditions, acne blemishes, upset stomach, cold and flu, diarrhea and impetigo.

Scope of Protection

As a general principle (according to the patents), this method will vaccinate safely against any allergen or antigen -- any substance which when introduced into the body creates antibodies (such as allergenic pollens, house dust, animal hairs, or micro-organism proteins).

Experimental studies in the patents listed in the references included "bacteria, viruses, proteins, animal tissue, plant tissue, spermatozoa, rickettsia, metazoan parasites, mycotic molds, fungi, pollens, dust and similar substances . . . exemplary antigens include: bacterial -- *Salmonella pullorum, Salmonella typhi, Salmonella parathypi, Staphylococcus, aureus, a Streptoccous agalactiae, g Streptococcus agalactiae, Staphyloccus albus, Staphylococcus pyogenes, E. Coli*, pneumocci, streptococci, and the like; viral -- Influenza type A, fowl pox, turkey pox, herpes simplex and the like; protein -- egg albumin and the like; tissue -- blood and sperm."

"In an experiment conducted at Notre Dame University's Lobund Institute, Impro [Products, Inc. substances] reduced tooth decay in laboratory animals as much as 87 percent."[35]

Protected according to the various patents were mice, cows, goats, chickens and pigs.

For allergy prevention, one can use a mixture of hair (cats, dogs, cattle), making a vaccine. Other allergens, such as pollens, can also be introduced, such that many other allergies can be beneficially affected.

This method is also good for chickenpox, cold sores, genital herpes, *Cryptocides sporidium*, and for anti-inflammatory conditions, as it is heavy with complement (C3B) and anti-complement, substances that assist in the destruction of invasive organisms.

Dialyzable Leuckocyte Extract-Transfer Factor
Beneficial Results[25]

Reported by Fudenberg and Pizza, Confirmed by Others

1. Familial T-lymphocyte dysfunction with severe recurrent infection.
2. Herpes infection
3. Cytomegalovirus infection
4. Candidiasis
5. Parasitic infection (e.g., *Pneumocystis carinae*,

cryptosporidiosis, etc.)

6. *Mycobacterium tuberculosis* infection refractory to antibiotics
7. Behcet's syndrome
8. Lupus erythematosus
9. Pemphigus vegetans (skin disease)
10. Wiskott-Aldrich Syndrome
11. Florence Nightingale Disease (aka Chronic Fatigue Immune Dysfunction Syndrome
12. Bone metastases after surgical removal of breast cancer
13. Bone metastases after surgical removal of kidney cancer
14. Guillian Barre
15. Amyotrophic lateral sclerosis (one subset)
16. Retinitis Pigmentosa (one subset, 50%; Dialyzable Leucocyte Extract-Transfer Factor does not reverse the disease but prevents additional visual loss)

Reported by Fudenberg and Pizza

1. *Mycobacterium fortuitum* infection
2. *Mycobacterium avian* infection
3. Alopecia totalis
4. Alzheimer's disease (one subset)
5. Autism (one subset, 70%)
6. Osteosarcoma (Dialyzable Leucocyte Extract-Transfer Factor prevents metastases to lungs)
7. Epidermal dysplasia (multiple cutaneous malignancies)
8. Certain food and chemical hypersensitivities
9 Burkitt's lymphoma, etc.

Reported by Others

1. Lepromatous leprosy
2. Leishmaniasis (Desert Storm disease)
3. Rat diabetes (Type I-immunologic) (trials in humans not yet reported, 1993)
4. Myasthenia gravis
5. Subacute sclerosing panencephalitis
6. Atopic dermatitis
7. Bronchial asthma
8. Recurrent otitis media
9. Varicella
10. Hepatitis B -- acute and chronic
11. Myasthenia gravis
12. Brucella
13. Asthma
14. Nasopharyngeal carcinoma
15. Stomach carcinoma
16. Colon carcinoma
17. Non-small cell lung carcinoma
18. Spontaneous abortions

Transfer Factor Sources[25]

Dialyzable Leucocyte Extract containing Transfer Factor "can be derived from peripheral blood lymphocytes, bovine lymph nodes, spleen and placenta of various species.

"It is present in all species thus far tested ranging from chicken, duck, mouse, rat, rabbit, burro, cow, goat, horse, dog, infrahuman primates, and many other species including man.

"It can cross species . . . lines without adverse effect or loss of potency.

"It can be prepared from peripheral blood lymphocytes obtained by venipuncture (60 ml blood for the average condition), by leukopheresis or lymphopheresis, and/or by cell lines from a donor with known high cell-mediated immunity for a given antigen, by sensitizing cell lines with dialyzable leucocyte extract containing transfer factor of a known specificity in great amounts and from placenta (*vide infra*)."[25]

Animal Transfer Factor Uses

• Bovine dialyzable leucocyte extract-transfer factor made against the parasite coccidioides protects not only cows but also mice from an LD 90 dose; bovine dialyzable leucocyte extract devoid of transfer factor has no protective effect;

• Bovine antigen-specific transfer factor is effective in treatment of human herpes infections;

• Bovine created for nematodes, *Haemonchus contortus*, *Trichostrongylus axei* infections is effective in sheep;

• Bovine dialyzable leucocyte extract, from both lymph nodes and colostrum, against virus and parasitic diseases, have been used in dogs (canine parvovirus), pigs (swine transmissible pharynogeolaryngeotracheitis), chickens (bursal disease, Newcastle's Disease, and other viral diseases);

• Coccidioides destroys $250 million per year of prize cattle in Texas. Lymph Node Leukocyte Extract (with Transfer Factor) can protect cattle against this infection, and also prevents mastitis in cows, and death from infection in newborn calves;

• Horse dialyzable leucocyte extract is effective against rheumatism in horses.

In Human Uses

• Bovine dialyzable leucocyte extract (with transfer factor) has been given repeatedly to humans without adverse reaction;

• Eradicated cryptosporidiosis in humans with diarrhea;

• Coccidioides derived transfer factor, eradicated diarrhea and eliminated ova and parasites from stools;

• Being used on 6,000,000 people in China to prevent acute and chronic infectious hepatitis;

• Many others conditions, as previously mentioned.

Major Source for Antigen/Allergen Specific Transfer Factor

• According to H. Hugh Fudenberg and Pizza,[25] "The potential for bovine colostrum-transfer factor treatment of human diseases is fantastic since one can obtain so much more dialyzable leucocyte extract at little cost." It is found free and in high concentration in colostrum; but can also be obtained from donors with high cell-mediated immunity to known antigens (cloning); or from human placentas, and also spleen from immunized pigs or ducks, or even humans who have a good cell-mediated immunity to the relevant antigens.

Where is Dialyzable Leucocyte Extract-Transfer Factor Used?

Because dialyzable leucocyte extract-transfer factor is so cheap, widespread, and easy to use, various countries outside of the United States use it, including China, Czechoslovakia, East Germany, Poland, Hungry. In Japan, the only high-wage country where it is used, forty Red Cross Centers provide dialyzable leucocyte extract-transfer factor from pooled leukocytes or normal healthy donors to 400 hospitals for use in a wide variety of conditions.

Use of dialyzable leucocyte extract-transfer factor does not cause hepatitis, but is effective against hepatitis, does not cause AIDS, and may be helpful in some of the diseases associated with AIDS.

In the late sixties, Herbert Struss, Ph.D., formerly Director of Research, W.E. Petersen Research Institute, St. Paul, Minnesota, working with the Borden Company of New York City, held a FDA IND for studying the use of bovine derived "Specific Serum Protein Capsules." Using in properly prepared cows 10 strains of *Streptococcus*, 2 strains of *Staphyloccocus* and 1 strain of *Diplococcus*, these lyophilized serum proteins derived from colostrum were prepared in 250 mg capsules, and contained the gamma globulin fraction of the antibodies and immunity which enabled some Rheumatoid Arthritis victims to overcome the disease, once again demonstrating a close relationship between an infectious microorganism and Rheumatoid Arthritis.

Seventy percent received marked benefit. "Cyril M. Smith, Minnesota physician, conducted a sample survey of 199 persons who used antibodies produced by cows in the treatment of arthritis symptoms. Smith reported that antibodies were successful in 56.8% of cases reported. This improvement occurred within 3 months. The greatest improvement was noted between the second and fourth weeks. However, in some cases it required more than 6 weeks before a marked improvement was noticed.

"Twenty-three percent who found relief from symptoms while taking antibodies experienced an increase in pain prior to their improvement. This "increase in pain" was most likely the Herxheimer Effect as summarized by Dr. Paul K. Pybus.[30] The great majority of the persons who experienced pain made marked improvement."[29] [Herxheimer postulated that whenever an organism more complex than a simple bacteria was killed inside the human body, then flu-like symptoms -- the Herxheimer Effect -- occurred. This effect is also called "Lucio's Phenomena" and "The Die-Off Effect."]

Despite outstanding success, the FDA halted the study for reason or reasons that remain unknown to this day.

According to Fudenberg and Pizza, the FDA "approved" bovine Transfer Factor for human use again in 1985 and bovine colostrum in 1980, said approvals appearing to be contrary to the present day non-approval experiences of some scientists and at least one company, all of whom prefer to remain unindentifed.

According to Fudenberg and Pizza, "Two federal courts (one a Medicare court in a suburb of Washington and the other a health and human services court in San Francisco) ruled in 1987 that in diseases where no prescription medicine exists Transfer Factor preparations are not experimental and furthermore ruled that insurance companies must reimburse the patients for the cost of Transfer Factor preparation."[25]

Brief Resume of Patents and Papers

(All described patents and papers are referenced..)

Abandoned Patent Petition (October 25, 1945)

A method is described for producing "medicinal agents of a biological nature which depend for their action on some phase or relation of immunity" from cows, to include protection against *H. pertussis, C. diptheriae, vaccinia virus.*

Canadian Patent Number 587,8549 (December 1, 1959)

Relates to "the production in the mammary glands of ungulates of high specific antibody or protective principle effective against a wide range of antigens," and isolation and separation of protective principle from milk, and to use of protective principle in prevention and treatment of disease in man and other animals. Examples used *Salmonella pullorum, Staphylococcus albus, Streptococcus agalactica, Aerobacter aerogenes, Escherichia coli, Salmonella typhi, Salmonella paratyphi.*

Immune Milk Treatment of
Rheumatoid Arthritis -- Review (June 1964)

Herbert E. Struss, Ph.D., W.E. Petersen Research Institute, St. Paul, Minnesota, reports on the use of *Staphyoccocus aureus, Streptococcus viridins, Streptococcus hemolyticus* and *Diploccus pneumoniae* in producing Immune Milk.

Supervised by B. Campbell at the University of Minnesota Medical School, individual case histories demonstrate complete remission of Rheumatoid Arthritis.

Cyril M. Smith, Minnesota physician, performed analysis of 199 cases with arthritis using Immune Milk, and reported success in 56.8% within 3 months.

The Herxheimer Effect

It was quite interesting that 23% of 113 persons who found relief from the symptoms experienced an increase in pain prior to their improvement, and the great majority of those who experienced this pain made marked improvement.

Exactly this same phenomena has been reported by Dr. Paul Pybus in *The Herxheimer Effect* published by The Arthritis Arthritis Trust of America/The Rheumatoid Disease Foundation,[30] when treating Rheumatoid Diseases with various anti-microorganism drugs. (See "The Herxheimer Effect," http://www.arthritistrust.org.)

History of the Use of Immune Milk
in the Treatment of Fall Pollenosis (1965)

Report by Herbert Struss, Ph.D. on open and controlled studies using Immune Milk.

In one study conducted by Jacob Blumenthal, M.D., Director of the Allergy Clinic, University of Minnesota, using dried skim milk powder produced by Dr. Struss, ". . . of 36 individuals using antibody milk, 15 apparently had good results, 9 had fair results, and in 12 there was no change." Three persons reported improvement using the control milk. There was a 4 standard deviation difference in favor of the immune milk over the control milk.

When specific antigen material was used to produce the immune milk, such as increasing the number of varieties of pollen extract of weeds and grasses, an increasing number of patients were protected.

Immune Milk in the Treatment of Poison Ivy (June 1965)

The cessation of itching and the stopping of blisters in addition to rapid healing in severe cases of poison ivy, using Immune Milk, are reported by Arthur E. Dracy of Brookings, South Dakota.

Patent Number 3,376,198 (April 2, 1968)

This patent covers the principle of injecting antigens (in non-pathogenic state) or allergens into the cistern of ungulates, immediately above the teats, before parturition, producing a therapeutically significant concentration of antibodies in milk in its natural state (not interfering with milk production) to be used to protect against various foreign allergens and antigens:

- Experimental subjects were cows, and the dead antigens were *Salmonella pullorum, Salmonella typhimurium, Salmonella parathyphi, Staphylococcus albus,* and *Herpes simplex* virus in mouse brain suspension.
- Experimental subjects were goats, and the dead antigen was *Salmonella pullorum.*
- Experimental subjects were chickens, and the dead antigen was *Salmonella pullorum.*
- Experimental subjects were pigs, and the dead antigen was *Salmonella pullorum*.

Patent Number 4,402,938 (September 6, 1983)

This patent covers the method of producing a food product containing colostrum and milk processed for stability and containing antigens and allergens selected from pollen, bacteria, virus, mold, allergens, blood from sick animals, sperm and toxins, producing an active fraction having a molecular weight of 1200 daltons or less.

Patent Number 4,816,563 (March 28, 1989)

This patent covers a process for inexpensively obtaining transfer factor from colostrum in large quantities, how to concentrate the transfer factor fractions contained in the colostrum (including centrifugation, extraction, precipitation, ultrafiltration, dialysis, chromatography and lyophilization), and how to use the transfer factor.

The transfer factor may be incorporated into food, pharmaceutical preparations or other compositions to prevent or treat disease associated with antigens for which the transfer factor is specific, such as *Mycobacterium bovis*, *Coccidioides immitis*, herpes simplex virus, human mump virus, bovine rhinotracheitis virus;

bovine parainfluenza virus, Newcastle's disease virus, Marek's disease virus, infectious bronchitis virus, laryngotracheitis virus, a protozoan or a cancer-related antigen.

In various scientific studies, protection and/or protective indicators found in the immune system, were clearly present for dairy cows and chickens

Unlike the process described in the other patents involving complement, described herein, this patent utilizes conventional state-of-the-art, routine vaccination procedures in the mammal, staged at appropriate intervals, to bring about the requisite transfer factor.

Patent Number 4,843,065 (June 27, 1989)

This patent covers the method of producing a product useful in treatment of bacterial and/or viral infections. The fluid contains no antibodies.

Patent Number 5,102,669 (April 7, 1992)

This patent seems to go considerably beyond the traditional procedure for developing homeopathic remedies.

a. Traditional homeopathic remedies place the raw product (allergen or dead antigen) in solution to produce a mother fluid. This mother fluid is then sequentially diluted to achieve one or more desired potencies, or dilution levels, any one or all of which might be used for various conditions.

b. This patent takes the mother solution and places it into the cistern of an ungulate which thereafter produces a second mother (from the ungulate). This second mother is then sequentially diluted to achieve one or more desired homeopathic remedies of various potencies.

Fabulous Findings! -- and
No Hankey Pankey or Placebo Effect Can be Alleged!

Mouse Tests

Groups of four mouse test subjects, using *Pseudomonas aurogenosa* challenges, were run, using categories of water, colostrum and milk as the raw materials to produce the second mothers, after which homeopathic remedies were prepared at 3X and 6X potencies for each category.

In brief summary of the first table in the patent, mouse survival was highest for 6X than for 3X for both colostrum and milk mother sources, but surprisingly, even higher results were obtained when both the 3X or 6X potency quantities administered were cut by one half or one quarter in both colostrum and milk, resulting in nearly 100% mouse survival rate, in most cases!

A second test showed similar results.

Cattle Herd Tests

One hundred and thirty cows having udder congestion and/or abnormal milk contributed milk samples. *Staphylococcus aureus, a Streptoccus agalactiae, g Streptococcus agalactiae*, and *E. Coli* were collected and used to make a first homeopathic mother from a healthy cow.

Homeopathic material was prepared to the 6X potency, whence these were bottled under 50 ml sterile conditions, of which ten 50 cc bottles were sent to the veterinarian.

"Each month the cows in a herd having high cell counts (disease indicator) are listed on the owners DH1A report for treatment. The high cell count cows in the herd were treated with 2-4 cc (ml) doses of the product orally in their feed at twelve-hour intervals with the results shown in the third table in the patent."

In the table, results showed that in most cases, a High Somatic Cell Count (SCC) of greater than 1,000,000 reduced to less than 200,000 within two weeks of treatment.

A similar study was performed, with similar results, using the cow's colostrum instead of milk.

Other Uses

Cured or protected according to all of these patents were mice, cows, goats, chickens and pigs.

Covered by Complement Patents: For allergy prevention, one can use a mixture of hair (cats, dogs, cattle), making a vaccine. (Many milk-producing farmers become allergic to cow's hair.) Other allergens, such as pollens, can also be introduced, such that many other allergies can be beneficially affected.

Covered by Complement Patents: It's also good for chickenpox, cold sores, genital herpes, *Cryptocides sporidium*, and for anti-inflammatory conditions, as it is heavy with complement and anti-complement (C3B), substances that assist in the destruction of invasive organisms.

Covered by Complement Factors: It is currently being used for treatment against candidiasis.

Covered by Complement Factors: Early work using the described principle for Rheumatoid Arthritis involved dead staphylococcus and streptococcus organisms injected as antigens into the cow's cistern. The successful results strongly support the theory of an infectious character of Rheumatoid Arthritis. As many forms of Rheumatoid Diseases and related diseases seem to have an infectious and/or allergenic component, such as ankylosing spondilitis, candidiasis, Crohn's disease, fibrositis, fibromyalgia, food allergies, rhinitis, and so on, this form of protection may be all-inclusive, inexpensive, and all-important.

Complement Factors: According to one spokesperson,[6] "The homeopathic remedy derived from this process has been found useful for various forms of arthritis.

Covered by Unknown: (Complements and/or Transfer Factor Patent) A trial court witness[17] for Herb Saunders (who treated Berkley Bedell of Lyme Arthritis Disease) suffering from multiple sclerosis reported very beneficial effects from the use of Saunders' specially prepared colostrum milk, and she, in turn, reported on another nearly crippled female multiple sclerosis patient who also had very beneficial effects from its use.

According to one source,[6] "A North Dakota support group uses this substance for multiple sclerosis with beneficial results." Early virological and immunological studies have suggested that multiple sclerosis is an auto-immune disease triggered by a viral infection.

A number of individuals have purchased their own milk cow and, using the principles first developed by University of Minnesota scientists, have been able to solve their otherwise intransigent health problems. One success in particular stands out: A retired dairy farmer in Minnesota had a daughter suffering from Epstein Bar Virus. He purchased a cow, injected his daughter's blood into the cow's cistern at appropriate intervals and, when the colostrum was collected, had his daughter drink it in small doses. After passing through a Herxheimer and 3 months of treatment, the daughter was wholly well again.

In a 1984 study reported in *Medical Microbiology and Immunology*[19] IgA-rich cow colostrum containing anti-measles lactoglobulin resistant proteases was orally administered to patients with multiple sclerosis. Measles-positive antibody colostrum was orally administered every morning to 15 patients with multiple sclerosis at a daily dosage of 100 ml for 30 days. Similarly, measles-negative antibody control colostrum (< 8) was orally administered to 5 patients. Of 7 anti-measles colostrum recipients, 5 patients improved and 2 remained unchanged. Of 5 negative (< 8) recipients, 2 patients remained unchanged and 3 worsened. These findings suggested the efficacy of orally administered anti-measles colostrum in improving the condition of multiple sclerosis patients ($P < 0.05$).

Beta-lactoGlobulin: In work supported by the National Institutes of Health and by Philip Morris Cos.,[11] "A modified version of

a protein extracted from whey blocked the AIDS virus from infecting cells in the test tube," according to Dr. Robert Neurath, head of the laboratory of Biochemical Virology at the Lindsley F. Kimball Research Institute of the New York Blood Center.

"Scientists modified a whey protein called beta-lactoglobulin to produce a substance called B69, which they discovered latched onto a protein structure called CD4 on the surface of cells." This prevented the AIDS virus from using CD4 as an entryway into the cells.

Dr. Jeffrey Laurence, an AIDS researcher at Cornell Medical College in New York, cautioned that HIV can infect some cells without using the CD4 gateway.

The Structural Research Center, Mobile, Alabama, headed by Walter Wilburn, Ph.D., has successfully accomplished the production of Lyme Arthritis antigen-specific immune milk from one of his certified scrappies-free goats. Using Stolle developed patents for innoculating specific antigens in chickens, eggs have also been produced which are sold under contract to the U.S. Army for incorporation in Army K-Rations.

Chisholm Biological Laboratory, 542 Legion Road, Warrenville, SC 29851, (8-3) 663-9618/9777, developed a number of antigen specific immune factors, including, but not limited to: HIV, *Pneumocystic carinii*, Human tuberculosis, *Borrelia burgdorferi* (Lyme Arthritis), Bovine Tuberculosis, Babesia, Ehrlichia, Epstein-Barr Virus (EBV), *Chlamydia pneumoniae*, Cytomegalovirus (CMV), Staphylococci, *E. Coli*, Herpes 1, Herpes 2, Human herpes virus 6 (HHV6), *Candida albicans*, Cryptosporosis, varicella zoster, and *Mycobacterium avian*.

Summary

• We've known for years that human babies who are breast fed have unusual disease resistance for several months, and are usually more allergen resistant in later life than their counterparts who have not been breast fed. By use of allergens and killed antigens an ungulate (or any mammal) will produce protective antibodies, transfer factors and complement in their cistern just before delivery of offspring. (As does the human mammal.) Colostrum, the first milk, has a ratio of helper T cells to suppressor T cells favorable for the exposure of higher quantities of transfer factor.

• The fluid containing antigen/antibody complexes and complements can be accumulated in the same volume as the milk itself, indeed, is contained in either the colostrum or the milk, which we can label and use as the "mother" for creating homeopathic remedies. The milk will have less of the protective factor than the colostrum, and the elements that suppress the expression of the protective factor will be greater in the milk than in the colostrum, but modern processes can concentrate the protective factors in either fluid. Or, we can screen out the resulting immuno-complexes through a sufficiently fine filter, and effectively use the resulting protective product in a similar manner. Transfer factors can inexpensively be isolated from colostrum, where it is found in higher quantities.

• Use of either the mother itself, or homeopathic remedies diluted 6X (1:999,999) from the mother, will produce protective antibodies in either mice or cows (and presumably other mammals), when using the complement bodies. No data is yet available to the writer on homeopathic transfer factor remedies.

Caution: Sales of whole whey products and homeopathic remedies based on the "whole whey principle" sold to patients are virtually worthless, according to the principles described, unless, by fortuitous and astronomical chance occurence there has been specific microorganisms or antigens used in their production which are identical to those affecting the purchaser.

This statement does not apply universally, as there can, indeed, be some utility in consuming products that have been developed from a range of antigen specific microorganisms. One must fully consider the source of the product and the conditions under which it has been transported, stored, and the claims made for its use.

• In the production of homeopathic remedies, as there is always a chance that foreign, dead antigens may be present in the first mother, however absurdly diluted, the first mother may be placed into the cistern of a cow, whence collected products may be used for a second mother.

• The second mother may also be diluted 6X (1:999,999), and will show the same protective qualities as did the direct use of the first mother or its homeopathic derivative.

• We've now reached some principle whereby the degree of dilution remotely connected to the first antigen or allergen (2nd mother) is significantly effective at 1 to 999,999, but even more effective when decreased in dosage by1/2 to 1/4. That is, it's not the antigen that creates the antibody that does the protecting, but rather some end product for which the antigen/antibody is merely a production intermediate! In this case, the end-product protective factor is possibly complement C3; or in some cases of non-homeopathic remedies,the described transfer factors.

• We're no longer dealing with homeopathic remedies based on the precept of antigen/antibody as a mother, but rather the mammals' ability to manufacture protective principles, a peptide, of something less than 1200 daltons, or perhaps an anti-complement, and/or transfer factors with a molecular weight >1200 daltons (Fudenberg). Apparently vaccinations deal with an intermediate of the protection cycle, rather than the protective principles themself.

• In homeopathic remedies, the probability, P, that an allergen or killed antigen may be found in any particular homeopathic vial (6X), approaches very close to zero.

• In homeopathic remedies, the probability, P, that an allergen or antigen may be placed in an ungulate's cistern from the first mother, and, coming out as milk fluids to form a second mother, be diluted to homeopathic strength of 1 to 999,999 (6X), and then be found in any one homeopathic vial used for human treatment, is exactly zero. (P = 0)

• It is unlikely that the FDA, the U.S. Department of Agriculture, or controlling pharmaceutical and agricultural industries will permit legitimate, unbiased tests of this product in the United States?

Why?

Because if these patents and papers represent genuine science, and actually produce the results described in the foregoing and the patents that follow, the whole financial basis of our modern pharmaceutical and agricultural industry can be seriously altered.

Final Understanding

Reporting in , *Certified Milk*,[24] R.M. Porter, Ph.D. wrote: "The fact that the udder is capable of producing antibodies against a wide variety of antigens is of major importance. This develops the possibility of using the lactoglobulin (antibody protein) of colostrum milk and milk produced later in the lactation (protective milk) for the health and welfare of man and animals. . . .

"When the dried lactoglobulin (lypholized) was resuspended in a physiological saline and administered intravenously at the rate of 0.5 g per 100 pounds of body weight . . . calves were protected when challenged with a lethal dose of E. Coli.

"Prophylactic and therapeutic use of protective milk or the isolated lactoglobulin has also been demonstrated in other animals. To study species differences in the absorption of antibodies from the gastrointestinal tract, milk produced against a polyvalent antigen was fed to such animals as the pig, mouse, chicken, guinea pig,

and humans. In all instances, a measurable titre was found in the blood within a few days after milk consumption began.

"It is estimated that the absorption of the anti-body is approximately 10 percent of that consumed. Even this amount is of extreme importance when considering the level of antibody that can be obtained in protective milks and the very small amount of antibody required for protection or that required to be of benefit therapeutically. We must remember that the amount absorbed depends upon the proper level and frequency of intake.

"The fact that antibodies and other proteins are absorbed from the gastrointestinal tract of the adult human and animals opens up an entire new vista in the use of antibodies in the medical and the veterinarian fields. The present value of protective milk and isolated lactoglobulin to the welfare of man is but a glowing ember in the light of what can be brought about by the cooperation of the medical field and the scientist in the dairy fields."

R. M. Porter, Ph.D. wrote these words in 1960!

Now I understand what they've been up against: Senator Tom Harkin, former Congressman Berkely Bedell, the patent holders, and the scientists working on this project this past half a century.

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Patents and Papers to be Appended Hereto

U. S. Patent Office October 25, 1945 628,987

According to Herbert Struss, Ph.D., Clearlake, Minnesota, Merck Chemicals, a German and American firm, was heavily in the horse serum business when Fleming found Penicillin, which pretty well wiped out the horse serum state-of-the-art of the times. The patent petition below, sponsored by Merck Chemicals, was never granted because of some confusion between the words "sow" and "cow." Merck Chemicals never pursued the patent further as this was the time when their horse serum business was wiped out by penicillin. The Germans, Struss says, were ahead of us in knowl-

edge of use of "Immune Milk."

Petition

To the Commissioner of Patients:

Your petitioner, August Holm, a citizen of the United States, residing at and whose post office address is R.F.D. No. 3, New Brunswick, in the County of Middlesex and State of New Jersey, prays that letters patent may be granted to him for the improvements in

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set forth in the annexed specification; and he hereby appoints Frank Wilen (Registration No. 12,428), Box 341, Brooklyn, N. Y., his attorney, with full power of substitution and revocation, to prosecute this application, to make alterations and amendments therein, to receive the patent, and to transact all business in the Patent Office connected therein.

/s/ August Holm

Specification

To all whom it may concern:

Be it known that I, August Holm, a citizen of the United States, residing at New Brunswick, in the County of Middlesex and State of New Jersey, have invented certain new and useful improvements in

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of which the following is a specification:

This invention relates to medicinal agents of a biological nature which depend for their action on some phase or relation of immunity.

When a preparation containing the microorganisms of an infectious disease, or a complex substance composed of the product of growth of microorganisms, or an animal product containing substances antagonistic to microorganisms or their products, is introduced within the body, an immunity may be imparted to the body; i.e., the body may be protected against the effects of these microorganisms or toxins thereof. Such immunity is called "acquired" immunity. In the "active" type of this immunity, the agents which actually do the protective work are created within the body. When such agents are introduced ready-formed from without, the immunity is called "passive."

Passive immunity is ordinarily produced by the injection of a serum (or fraction thereof) containing an immune factor or factors (e.g., antibodies) which directly antagonizes the invading pathogen or a toxin thereof. (For simplicity, the term "factor" is employed hereinafter in the sense of "factor or factors.") Such "immune" sera are obtained by actively immunizing the larger domestic animals, i.e., by injecting the animals with the appropriate antigen, and then bleeding the animals to secure the serum. The sera are usually treated to remove as many inactive substances as possible, leaving the immune factor or factors in a concentrated form.

Infant mortality due to infectious diseases is a recognized public-health problem of great importance. For example, in the year 1941 there were in the United States over 30,000 deaths of infants under one year from whooping cough, dysentery, influenza, pneumonia, diarrhea, enteritis, diptheria, scarlet fever, tetanus, or menigitis; but till now there have been available no medicinal agents which could be expected to decrease such infant mortality.

It is known that certain immune factors in the mother are transferred through the placenta. The immunity conferred, however, lasts only for a short time. It is known also that this immunity is augmented by a supply of the immune factor through the mother's milk. Prior to this invention, there was no way (other than by injection of antigens or combined antigens) to augment the immunity of the non-breast-fed infant; but immunization by injection has certain obviously-undesirable features, and response to active immunization is absent or almost absent in very young infants.

The preparations of this invention essentially comprise the immune factor of the milk of a bovid, especially a cow, that has been actively immunized with the antigen corresponding to the disease against which passive immunity is to be conferred. It has been found: (a) that an appreciable proportion of such heterologous immune factor is absorbed into the blood stream without destruction when ingested by normal human beings (including infants); and (b) that this absorbed heterologous immune factor is capable of conferring passive immunity upon the human being, without undesirable reactions (hypersensitivity) to the normal human being.

The immune factor is present in the whey portion of the milk, and that portion is desirably fractionated for concentration of the immune factor (which is in the lactoglobulin fraction); but the whey or the immune milk itself may be employed as the medicinal agent, either in liquid or dried form.

The concentration of the immune lactoglobulin may be effected by any of the various methods heretofore employed for the concentration of the immune globulin of sear, e.g., by fractionation with ammonium sulfate or other salting-out salts, fractionation with alcohols, fractionation by enzymatic digestion (cf. Gerlough patent 2,368,464) or fractionation with polyuronides (cf. Gerlough patent 2,161,861).

Preferably, the bovid is actively immunized with the antigens corresponding to at least two diseases, to provide a polyvalent-immune preparation. (Such a preparation may also be provided by combining separately produced monovalent-immune preparations; but the correspondingly decreased potency of the preparation would necessitate the administration of proportionately larger quantities, which might be inadvisable, especially when three or more monovalent-immune preparations are combined).

After the desired degree of active immunization is attained (i.e., when the potency of the bovid's serum has reached a level indicating an adequate potency in the milk), the milk is collected, and (preferably) processed to concentrate the immune factor. The immune whey, or the further concentrated immune fraction thereof, is preferably made substantially-dry (e.g., freeze-dried) to provide it in a form that is stable and suitable for ready "solution" in water, milk, or other fluids used for infant feeding, or for ready admixture with cereals, babyfood, or the like. (Separate administration in an aqueous medium is preferred from the standpoint of maximizing absorption of the immune factor.) The amount to be administered depends, of course, on the potency of preparation; i.e., it should be sufficient to confer upon the blood serum of a normal human being the ability to react positively to the antigens used for the active immunization of the bovid.

The immune whey or further concentrated immune fraction thereof may be packaged and distributed in "aqueous solution" form, either in single-dose or multi-dose containers. The preferred substantially-dry (e.g., freeze-dried) form also may be packaged and distributed in single-dose as well as multi-dose containers, which, desirably, should be moisture proof (a suitable container for the single dose being the aluminum-foil packet known as Uni-Wrap, the packaging of the dose being effected as described in patent 2,372,406).

The immune whey or further concentrated immune fraction thereof may be incorporated (in suitable proportion) in the various preparations used for infant feeding; e.g., in milk-modifiers (preparations intended for incorporation in bovine milk to provide a simulated human milk or for other specialized purposes), powdered milk products, and vitaminic products.

The following examples are illustrative of the invention:

Example 1

Immunization

(a) A phenol-Merthiolate killed *H. pertussis* vaccine, containing 10 billion organisms per ml., prepared as for human immunization [Am. J. Hyg. 29:133 (1939)] is injected intravenously into cows in increasing amounts for 5 days of each of two weeks according to the following schedule (in ml.): first week, 0.6, 1, 2, 3, and 3; second, 3, 4, 4, 5, and 5. The number of organisms injected is then increased rapidly according to the tolerance of the cows, until a sustaining dose is reached; and the immunization is continued at that level during the period in which the immune milk is to be produced.

(b) A regular diptheria toxoid prepared as for human immunization is injected intradermally into the same cows in increasing amounts for two weeks according to the following schedule (in ml.): first week, 5,5, and 5 of a 1/20 dilution, and then, 5 of a 1/10 dilution; second, 1,1,2,2, and 3 of undiluted. The amounts of diptheria toxoid injected intradermally are then increased to a total of 15cc. per week, and further injections are made subcutaneously in increasing amounts to a total of 50cc. per week, with or without the addition of calcium chloride, according to the tolerance of the cows. If the tolerance is good, subcutaneous injections with routinely prepared diptheria toxoid [J. Immunol. 22:93 (1932)] may be given in increasing amounts during the period in which the immune milk is to be produced.

(c) A regular vaccina virus vaccine prepared as for human immunization against smallpox is injected intradermally into the same cows in increasing amounts for four weeks according to the following schedule (in ml.): first week, 0.1; second, 0.1; third, 0.1 and 0.3; fourth, 0.3 and 0.5. The amounts of vaccina virus vaccine injected intradermally are then increased gradually (or virus vaccine is given subcutaneously) according to the tolerance of the animals during the period in which the immune milk is to be produced.

Trial bleedings of the cows are taken at intervals, and the serum is assayed for antibodies against *H. pertussis*, diptheria toxin, and vaccina virus. When potency of the serum has reached a level indicating the desired potency in the milk, collection of the milk is started and the (pooled) immune milk is processed as detailed in the following section.

Concentration

The immune milk is centrifuged to separate the cream; and 3.8 liters normal hydrochloric acid is slowly added with constant stirring to 76.5 liters of the immune skim milk (the pH then falling to about 4.6). The grandular casein precipitate formed is removed by filtration through a course filter, 69.9 liters of immune whey being recovered. This is adjusted to a pH of about 7.1 with 2750cc. of normal sodium hydroxide solution; and 16.9kg. of ammonium sulfate is added to bring the solution to 40% saturation and to a pH of about 6.9. The crude immune-lactoglobulin precipitate is separated by filtering or centrifuging, and the excess mother liquid is removed from the precipitate by absorption with filter (or other absorptive) paper. The precipitate (about 525g.) is dissolved in water to make an approximately 3% solution, and filtered clear; and to 8220cc. of this crude immune-lactoglobulin solution, adjusted to a pH of about 7 with sodium hydroxide, is added 5060cc. of saturated ammonium sulfate solution, to bring the solution to 35% saturation. This resulting precipitate is separated by filtering or centrifuging, and excess moisture is removed by absorption and pressing; the precipitate is then dialyzed until salt-free; and the resulting solution of concentrated immune lactoglobulin is then freeze-dried.

(The immune-lactoglobulin may be obtained in a higher state of purity but lower in yield, by reprecipitating the crude immune lactoglobulin in a lower range of ammonium sulfate concentration, for example at about 25-33% saturation.)

Example 2

Alternative Concentration

An immune whey obtained as described in the "Concentration" section of Example 1 is neutralized (pH 6.9-7.1), and ethanol is added to a concentration of 25% at -5^0 C.; and the resulting precipitate is removed by centrifuging. The crude immune-lactoglobulin thus obtained is redissolved in water, the insoluble material is removed by centrifuging and filtering, and the immune-lactoglobulin is reprecipitated at -5^0 C. and 20% ethanol concentration. This method of fractionation gives higher yields than ammonium sulfate fractionation described in Example 1.

Example 3

The crude immune lactoglobulin precipitate obtained as described in the "Concentration" section of Example 1 is dialyzed until salt-free, and then diluted to about 3% protein concentration at pH 6.9-7.1 and at a sodium chloride concentration of about 0.04 molar. The thus-treated solution is then filtered clear, and ethanol is added to a concentration of 25% at -5^0 C.; and the precipitate is separated by centrifuging. This method of concentration gives an almost quantitative yield of a 90% pure immune-lactoglobulin.

Other antigens may be used in place of or in addition to those mentioned hereinbefore for the active immunization, to obtain preparations for conferring the corresponding passive immunity upon human beings by oral administration. These additional antigens, which may be used either alone or in combinations of two or more (with those mentioned hereinbefore) comprise tetanus toxin, and toxoid, scarlet fever streptococcus toxin, streptococcus vaccine, pneumococcus vaccine, meningococcus vaccine, dysentery antigen, typhoid antigen, human influenza virus, poliomyelitis virus, and other antigens corresponding to pathogens for human beings, especially infants.

The preparation of this invention may, of course, also be used for the treatment (prophylactic passive immunization) of children and adults; but the primary advantage (utilizability where active immunization by injection is undesirable or unfeasible) is not present in these cases.

The invention may be variously otherwise embodied within the scope of appended claims.

Claims

1. A preparation for conferring passive immunity upon human beings by oral administration, essentially comprising the immune-lactoglobulin fraction of the milk of a bovid that has been actively immunized with a non-infectious antigen corresponding to the disease against which the passive immunity is to be conferred.

2. A preparation for conferring passive immunity upon human beings by oral administration, essentially comprising the immune-lactoglobulin fraction of the milk of a cow that has been actively immunized with a non-infectious antigen corresponding to the disease against which the passive immunity is to be conferred.

3. A preparation for conferring passive immunity upon human beings by oral administration, essentially comprising the immune-lactoglobulin fraction of the milk of a bovid that has been actively immunized with non-infectious antigens corresponding to at least two diseases against which passive immunity is to be conferred.

4. A preparation for conferring passive immunity upon human beings by oral administration, essentially comprising a polyvalent-immune-bovid-lactoglobulin.

5. A preparation for conferring passive immunity upon hu-

man beings by oral administration, essentially comprising the immune-lactoglobulin fraction of the milk of a bovid that has been actively immunized with a *H. pertussis* vaccine.

6. A preparation for conferring passive immunity upon human beings by oral administration, essentially comprising the immune-lactoglobulin fraction of the milk of a bovid that has been actively immunized with a *C. diptheriae* antigen.

7. A preparation for conferring passive immunity upon human beings by oral administration, essentially comprising the immune-lactoglobulin fraction of the milk of a bovid that has been actively immunized with vaccinia virus vaccine.

8. A preparation for conferring passive immunity upon human beings by oral administration, essentially comprising the immune-lactoglobulin fraction of the milk of a bovid that has been actively immunized with *H. pertussis* vaccine, a *C. diptheriae* antigen, and vaccinia virus vaccine.

9. A preparation for conferring passive immunity upon human beings by oral administration, essentially comprising the milk of a bovid that has been actively immunized with a non-infectious antigen corresponding to the disease against which the passive immunity is to be conferred.

10. A preparation for conferring passive immunity upon human beings by oral administration, essentially comprising the whey of the milk of a bovid that has been actively immunized with a non-infectious antigen corresponding to the disease against which the passive immunity is to be conferred.

11. A preparation for conferring passive immunity upon human beings by oral administration, essentially comprising the immune-lactoglobulin fraction of the milk of a bovid that has been actively immunized with the antigen corresponding to the disease against which the passive immunity is to be conferred.

12. A preparation for conferring passive immunity upon human beings by oral administration, essentially comprising the substantially-dry immune-lactoglobulin fraction of the milk of a bovid that has been actively immunized with a non-infectious antigen corresponding to the disease against which the passive immunity is to be conferred.

13. A substantially-dry immune-bovid-lactoglobulin.

14. A substantially-dry polyvalent-immune-bovid-lactoglobulin.

15. The method of conferring passive immunity upon human beings, which comprises orally administering a preparation essentially comprising the immune-lactoglobulin fraction of the milk of the bovid that has been actively immunized with a non-infectious antigen corresponding to the disease against which the passive immunity is to be conferred.

16. The method of producing a preparation for conferring passive immunity upon human beings by oral administration, which comprises actively immunizing a bovid with a non-infectious antigen corresponding to the disease against which the passive immunity is to be conferred, and collecting the milk of the immunized bovid.

17. The method of producing a preparation for conferring passive immunity upon human beings by oral administration, which comprises actively immunizing a cow with the antigen corresponding to the disease against which the passive immunity is to be conferred, and collecting the milk of the immunized cow.

18. The method of producing a preparation for conferring passive immunity upon human beings by oral administration, which comprises actively immunizing a bovid with non-infectious antigens corresponding to at least two diseases against which passive immunity is to be conferred, and collecting the milk of the immunized bovid.

19. The method of producing a preparation for conferring passive immunity upon human beings by oral administration, which comprises actively immunizing a bovid with a non-infectious antigen corresponding to the disease against which the passive immunity is to be conferred, collecting the milk of the immunized bovid, and concentrating the immune-lactoglobulin fraction thereof.

20. The method of producing a preparation for conferring passive immunity upon human beings by oral administration, which comprises actively immunizing a bovid with *H. pertussis* vaccine, a *C. diptheriae* antigen, and vaccinia virus vaccine, and collecting the milk of the immunized bovid.

In witness whereof I affix my signature.

/s/ August Holm

Oath

State of New Jersey }ss.
County of Middlesex

August Holm, the above-named petitioner, being duly sworn, deposes and says that he is a citizen of the United States and a resident of New Brunswick, in the County of Middlesex and State of New Jersey, that he verily believes himself to be the original, first, and sole inventor of the improvements in

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described and claimed in the annexed specification; that he does not know and does not believe that the same was ever known or used before his invention or discovery thereof, or patented or described in any printed publication in any country before his invention or discovery thereof, or more than one year prior to this application, or in public use or on sale in the United States for more than one year prior to this application; that said invention has not been patented in any country foreign to the United States on an application filed by him or his legal representatives or assigns more than twelve months prior to this application; and that no application for patent on said improvements has been filed by him or his representatives or assigns in any country foreign to the United States.

/s/ August Holm

Sworn to and subscribed before me this 25th day of October 1945.

Lucionne Brown
Notary Public of New Jersey

Canadian Patent Office **587,849**

Issued Dec. 1, 1959
Patent No. 587,849
Production of Protective Principle
William E. Petersen and Berry Campbell,
St. Paul, Minnesota, U.S.A.
Application November 9, 1955,
Serial No. 696,174
In the United States April 7, 1955
14 Claims --- No drawings

This invention relates to the production in the mammary glands of ungulates of high specific antibody or protective principle effective against a wide range of antigens. This invention also relates to the isolation and separation of protective principle from milk and to the use of protective principle in the prevention and treatment of disease in man and other animals and in the preparation and purification of biologics, proteins, antigens, and the like.

The importance of the colostrum of the cow as a source of antibodies in the newborn calf has been recognized for many years and has been extensively studied. The work leading to this invention has been toward the application of these known basic phenomena to a wider field of usefulness than is possible in what might be termed the natural mechanisms. Upon initial inquiry it was discovered that the site of antibody production in the bovine udder is

the interstitial plasma cells. These cells were found to vary in number with antibody production. It was then discovered that the animal could be caused to produce chosen antibodies by infusion into the udder of specific species of microorganisms, dead or alive, and by similar application of protein antigens and tissue antigens, normal or pathological. It was discovered that the amount of return of specific immune bodies in the milk of animals so treated was heightened by booster applications of the antigens, locally and systemically.

Practical application of the immune material in the prevention and treatment of disease in man and other animals was made possible by our discovery that either the ingestion of the milk containing this material or perfusion into the hind-gut allowed absorption of the immune bodies into the bloodstream of older animals as well as the newborn and of animals of different species from the donors. Parenteral applications of the antibody or protective principle have been made in animals of the same species and different species from the donor.

The fraction of the milk bearing the immune material may be separated by centrifugation at specified pH and temperature conditions. The antibody fortified milk from ungulates stimulated according to this invention may be preserved by pasteurization or by drying.

A principal object of this invention is to provide a method of inducing high specific antibody or protective principle against a wide range of antigens in the mammary glands of ungulates.

Another major object of this invention is to provide a method of applying immunizing bodies from the ungulate mammary gland in medicine and animal husbandry.

A further object of this invention is to provide as a new composition of matter, high titer milk, rich in specific protective principle against any wide variety of antigens and combinations of antigens.

Still another object of this invention is to provide a method of isolation and separation of antibodies or protective principle from milk stimulated mammary glands of ungulates.

Other objects of the invention will become apparent as the description proceeds.

To the accomplishment of the foregoing and related ends, this invention then comprises the features hereinafter fully described and particularly pointed out in the claims, the following description setting forth in detail certain illustrative embodiments of the invention, these being indicative, however, of but a few of the various ways in which the principles of the invention may be employed.

Production of Protective Principle

High specific antibody in the milk of ungulates (particularly cows, goats, sheep, etc.) is produced against any antigen by introducing such antigen into the udder of the animal. Specific antibody in the milk is produced from the introduction of the antigen into the teat canal of the animal at any time. However, the highest antibody response occurs following introduction of the antigen during the animal's dry period and especially following a series of introductions, known as boosters, spaced over a period of time.

Although the amounts of antigens introduced, the frequency (time interval) and the number of booster doses may vary widely, the highest antibody response results from the injection of a plurality of doses of increasing amounts into the udder of an animal in its dry period over a period of several weeks.

The size and concentration of the antigen doses are not critical but are selected for convenience. It has been found that increasing or decreasing the size of the antigen injection does not produce a corresponding increase or decrease in the protective principle titer of the resulting milk. The antigenic substance may be injected at any time but in the case of a non-lactating cow it is often preferred for convenience that the antigen be introduced toward the end of the gestation period. Thus, for example, the initial injections can conveniently be given from about two to eight weeks before parturition.

Booster shots, when given, may likewise be spaced to suit the convenience of the operator except that the injections should be made frequently enough that an anaphylactic reaction does not occur. For most species that time is less than about ten to fourteen days. To avoid local irritation and congestion it is usually preferred that booster injections not be given more frequently than every other day. The antigenic substances are suspended in liquid medium for injection, such as, for example, sterile physiological saline solution. The injection is made into the duct system of the udder through the teat meatus and into the gland cistern. The udder may, if desired, be massaged for better penetration of the antigen into the duct system of the udder.

Where injections of antigen are made in the dry cow the protective principle is present in the milk immediately upon freshening. Booster injections are then given intravenously, intramuscularly or subcutaneously to maintain production of protective principle at a high level.

In the lactating cow initial injection and booster injections may be made directly into the udder. The protective principle becomes apparent in the milk from about two days to two weeks after the initial injection varying somewhat upon the particular antigen employed. For example, *Streptococcus agalactica* was noted in the milk on the tenth day following inoculation of a lactating cow.

The antigenic substances which are employed in the practice if this invention for the production of protective principle include bacteria, viruses, proteins, mycotic molds and fungi, tissue, pollen, dust and similar substances which are antigenic. Exemplary antigens include: Bacterial: *Salmonella pullorum, Salmonella typhi, Salmonella parathphi, Staphylococcus aureous, Staphylococcus albus, Staphylococcus pyogens*, pneumococci, streptococci, and the like; Viral: Influenza Type A, fowl pox, turkey pox, herpes simplex, and the like; Protein: egg albumin, mouse tissue, egg embryo tissue and the like; Tissue: blood and sperm. It is to be understood that these materials are merely representative of the almost infinite number and variety of antigenic substances against which specific antibodies or protective principle can be produced in the ungulate udder. The expressions "antigenic substance" and "antigenic material" are used to designate materials which are antigenic in and of themselves and also non-antigenic materials which act as antigens in the presence of adjuvants. Antigenic disease organisms are specifically included within these expressions.

Example 1

The experimental subject was a Jersey cow, 5 weeks before parturition. The antigen killed was *Salmonella pullorum.* The initial dose of antigen was injected into the teat canal, 1ml. of antigen per quarter containing approximately 5 billion organisms. The first booster dose was injected one week later, 1ml. antigen per quarter containing about 10 billion organisms. Subsequent booster shots of 1ml. per quarter containing increasingly larger concentrations of the antigenic material, about 20, 30, and 40 billion dead organisms, respectively, were injected at one week intervals. Milk following parturition agglutinated the antigen at more than 100,000 dilutions.

The antibody or protective principle in the milk decreases rapidly following parturition, from agglutination at more than 100,00 dilutions immediately following parturition to agglutination at only 1,000 dilutions in four weeks. The level of the protective principle may be brought up and maintained by the systematic administra-

tion of antigen. Following parturition booster doses of the antigen may be administered by parenteral injection of the antigenic material, intravenously, intramuscularly or the like. Postpartum boosters cannot be injected in the teat canal but must be made parenterally to avoid an allergic reaction.

Example II

The procedure of Example I was repeated on a different cow with only exception being that the doses of antigen injected in both the initial injection and the boosters were only one-tenth as concentrated as those used in Example I. The resulting milk was high in protective principle, there being no apparent difference from the milk of the first example.

Example III

Protective principle was produced in a lactating cow by injecting *Streptococcus agalactica*. The initial injection was made in one quarter and consisted of a 5ml. dose containing about one billion organisms. This cow showed a negative reaction before the initial administration of the antigen. The protective principle appeared in the milk on the tenth day. At the end of fifteen days the milk had a high titer as revealed by precipitation reaction. Reinjection of antigen into the same quarter on the sixteenth day produced a strong allergic reaction.

Example IV

Aerobacter aerogenes was administered to a lactating cow in an initial injection of 5ml. containing about two billion organisms made in one quarter. The titer of the milk of the day of injection was 1:20. Sixteen days later the titer was 1:5120.

Example V

Escherichia coli was injected in a lactating cow in an initial intra-mammary injection in one quarter of 5ml. containing about 200 million bacteria. The milk fourteen days later showed complete agglutination in 1:20 dilution.

Example VI

Staphylococcus aureous was injected into the udder of a lactating cow. The cow was not milked for one day and then milking was resumed at regular intervals. Milk ten days after injection showed complete agglutination at 1:10 dilution.

Example VII

To show the production of protective principle against specific combination of antigenic substances a mixture of approximately equal number of Pneumococcus, type 1; Pneumococcus, type 2; *Salmonella typhi; Salmonella paratyphi* and *Staphylococcus albus* were injected into the udder of a cow two weeks before calving. A similar mixture was given as a booster one week later. The milk after calving showed a strong reaction for antibody against all of the injected species.

Example VIII

A 90mg. dose of standard fowl pox virus in 3ml. of water was injected into one quarter of a cow. Growth of virus in the quarter was shown by reaction five days later.

Example IX

To further illustrate the administration of virus 1ml. of standard herpes simplex was injected into one quarter of a cow resulting in production of antiviral protective principle.

Example X

Two ml. of egg white was injected into one quarter of a lactating cow. There was no reaction at the time of administration and the precipitation test was negative. Twelve days later the milk showed a strong precipitation reaction. On the following day injection of an additional 2ml. of egg white into the same quarter brought about a violent allergic reaction.

Example XI

Production of protective principle in goats was carried on by giving daily infusions of 1 ml. of a suspension of *Salmonella pullorum* via the teat canals to a pregnant goat. The daily infusions were given over a period of more than four months prior to parturition.

The antibody or protective principle may be preserved in pasteurized milk, condensed milk, dried milk and in gamma globulin isolated from the milk. Pasteurization temperatures must be carefully controlled. Normal pasteurization (i.e., 140 degrees F. for 30 minutes) has no adverse effect upon the protective principle. Care must be taken to prevent the temperature from rising for any appreciable period of time. For example, when pasteurization is carried out at 155 degrees F. the protective principle in the milk was found to drop one-half. Cooling of the pasteurized milk must be prompt in order to preserve the protective principle. Pasteurization may be accomplished by known "flash" or "holding" methods. The milk containing protective principle may be condensed under careful temperature control. Dried milk containing the antibody or protective principle is preferably prepared from the non-condensed product. However, the condensed milk may be used if at first condensed carefully at low temperatures to avoid destroying of the protective principle. Drying can be accomplished under either spray or roller drying processes under properly controlled conditions in order to preserve the protective principle. High temperatures per se are not detrimental to the protective principle except when sustained for a period of minutes. Thus, the milk may be dried in a dryer in which temperatures of 300-400 degrees F. are achieved but the milk is at these temperatures only for an instant.

A proliferating virus can be administered to the udder in a two-stage operation. The first inoculation is made in the normal manner. The second inoculation is then made in milk resulting from the first, with the accompanying tissue antigens diluted out.

This screening procedure is illustrated as follows:

Example XII

A cow was infused into the teat canals with herpes simplex virus in mouse brain suspension. The cow was lactating and was regularly milked thereafter. The next day the milk showed a positive Whiteside test. On the second day following the inoculation the milk was used for injection into the udder of a dry cow via the teat canals. The result was the transfer of the virus without the mouse brain antigen.

Application of Protective Principle

The antibody or protective principle which is the product of this invention is useful in a variety of ways. It has been discovered that the protective principle or antibody is absorbed into the system after the milk from stimulated udders has been ingested or administered by proctoclysis. The isolated and separated protective principle may be administered orally, rectally, parenterally and topically. The protective principle is useful in the immunization and treatment of humans and other animals.

The application of the protective principle of this invention is illustrated by the following examples:

Example XIII

The experimental subjects were four adult humans. The protective principle was prepared generally according to the procedure of Example I, the resulting milk containing antibody against *Salmonella pullorum* bacteria. All of the subjects were negative by agglutination test prior to ingestion of the milk. The subjects consumed from about one pint to one quart of the milk containing the protective principle. All absorbed the antibody from their digestive tracts into their blood streams as determined by the agglutination test. One of the subjects consuming one quart milk daily developed an agglutination titer in the blood diluted tenfold.

Example XIV

The protective principle against *Salmonella pullorum* was also applied to fowl. The experimental subjects were six adult chickens all negative to the *Salmonella* antibody test. After one feeding of the milk containing the protective principle all of the chickens developed a strong positive reaction.

Example XV

A further application of the protective principle of this invention was made to chickens and showed positive protection afforded by the protective agent. Twenty day old chicks were divided into an experimental group of ten and a control group of ten. The experimental chicks were fed milk produced according to this invention with a high titer (1:1,000) against *Salmonella pullorum*. *Salmonella pullorum* is a chicken disease organism. The controls were fed milk with no such specific antibody. During the first day of the experiment the two groups were injected intracardially with an infusion of live *Salmonella pullorum* in broth. The mortality of the controls was heavy, the fifth chick being dead in 24 hours while in the experimental group the fifth death did not occur for 120 hours. The general state of health of the control chicks was poor as compared with the experimental group. This is a severe test of the protective principle since the organisms were injected directly into the hearts of the experimental subjects, a mode of transmission which would never be encountered normally. Chickens as a species are far removed from the cow. Yet the protective principle produced in the cow is readily conveyed by the milk into the blood stream of the chickens by absorption through the digestive tract.

Example XVI

The protective principle was applied to bovine subjects. The subjects were tow 5-month-old calves with fully functional rumens. The calves were negative to the *Salmonella* antibody test. After two feeds of the milk containing *Salmonella pullorum* protective principle they developed strong positive agglutination reaction in the blood.

Example XVII

Porcine animals were also tested. The experimental subjects were two mature pigs weighing about 200 pounds each and negative to the antibody test. After one feed of milk containing protective principle against *Salmonella pullorum* both pigs developed a weak reaction. After two feeds of milk they showed strong reaction in the blood.

Example XVIII

A 90 kg. adult man, never exposed to *Salmonella pullorum*, and with no demonstrable blood titer was injected rectally with a solution of 1.4 grams of lyophilized gamma globulin fraction of immune colostrum produced according to this invention which had a titer of 1:1,000. Three quarters of an hour later no agglutinating antibodies in the finger tip blood could be demonstrated and 0.6 grams more of the same material in solution was injected. On the following day a detectable reaction to 1:5 dilution was obtained. This same result was repeated on the second day following the injection.

Example XIX

Lyophilized fraction of colostrum was added to a calf rectally as follows: From the colostrum of a cow in which protective principle against *Salmonella pullorum* had been produced according to this invention, a high titer fraction was isolated by cold precipitation with alcohol. Fifteen grams of this was administered in 50ml. of water by infusion into the rectum of a two-week-old calf. The anus was secured for 8 hours with a purse-string suture. The calf was then bled and its serum showed, by a positive agglutination test to *Salmonella pullorum* that absorption into the blood stream had occurred.

The experiments with the humans, calves and pigs show that with continued ingestion of the milk containing the antibody, the levels of the protective agent continue to increase in the blood. Experiments with humans and calves also show that the protective principle is absorbed from the rectum. The rate of absorption from the rectum is less than from the anterior part of the system. Rectal absorption may be resorted to, however, if oral administration is contra-indicated. The high antibody or protective principle containing material may be applied topically (unction) in treatment of local exacerbations due to allergy.

Salmonella pullorum antigen has been used in the experimental work described in the above examples because it is relatively harmless to the experimental subject; it is readily available, easily identified and its absorption into the system of the subject can be readily traced by the agglutination test. It is to be understood, however, that this specific bacterial antigen is used for illustrative purposes only and the invention is not so limited.

It is recognized that gamma globulin produced in one animal is antigenic under some circumstances in other species. For example, cow gamma globulin is antigenic in non-bovine species. There are occasions, however, for using isolated gamma globulin from cows with high specific antibody or protective principle parenterally in other species. For example, gamma globulin from cows' milk containing protective principle against hog cholera may be administered to pigs and hogs.

Gamma globulin with high protective principle produced according to this invention has real use in the treatment of other animals of the same species in which it is not antigenic, for example, separated gamma globulin from cows is useful in calves and other cattle.

With the discovery that the protective principle or antibody can be absorbed from the digestive tract and that it is possible to produce specific antibody in milk against most, if not all, antigens by proper treatment of ungulates to stimulate such antibody or protective agent development, avenues are open for a new approach to the prevention and treatment of disease in both man and other animals.

The initial step is the production of specific protective principle against a mixture of all known antigens for either human or lower animals or the production of one specific protective principle such as antibody against a specific antigen, for example, rag weed pollen.

Since the mammary gland, particularly of the cow, will produce specific antibody or protective principle antibody or protective principle against any antigen, bacterial, viral, mucotic, protein and the like, milk may be prepared with protective principle useful against infectious disease organisms and other antigens in humans and lower animals. Specifically prepared milk containing specific antibodies against specific although rare diseases and other specific antigen induced conditions may be produced. For example, protection to hay-fever sufferers from rag weed pollen is offered by consumption of milk with a high protective principle against rag weed pollen.

As the literature indicated antigenicity of tumors, when such an antigen is isolated and injected into the udder, specific antibody may be produced against it. When milk containing such specific protective principle is ingested or otherwise administered, it may retard or even cause complete involution of such a tumor.

Dried milk containing specifically produced antibody or protective principle may be made up as a poultice in the treatment of contact allergies. Isolated gamma globulin from milk containing protective principle may be moistened and similarly applied as a poultice. For instance, milk is produced containing antibody against the poison oak or poison ivy antigen and is applied to the skin

surface that has been contacted by one of these antigens to neutralize the poisonous principle.

An important application of the protective principle of this invention in the field of animal treatment is furnishing protective colostrum for calves. At the present time it has been estimated that some 20% of all calves born alive die within the first few weeks of life. Death is caused principally by infectious organisms against which antibodies may be developed. Mixed antigens of all of the common infectious diseases that kill calves are prepared and injected appropriately into the udders of dry cows. The colostrum from such stimulated udders is dried, packaged and made available to feed calves immediately after birth to give the calves the necessary level of antibodies to carry them through the critical part of their life.

For administration of the protective principle of this invention to humans a preferred method is incorporation into milk and other dairy products. Since the protective principle agglutinates at dilutions as great as 100,000 the original milk containing the protective agent can be greatly diluted with non-protective milk and distributed and fed in this form. Ordinary milk may thus be given a high protective level against specific antigenic materials. The amount of dilution is dependent upon the titer of the protective principle enriched milk and the required level of antibodies needed for effectively combatting the specific antigen and the like. As an example, a gallon of the original high-titer (say, 1:100,000) milk from a cow treated to produce protective against any particular antigen may be admixed with 99 gallons of ordinary non-protective whole milk to produce 100 gallons of milk of sufficiently high titer (1:1,000) to be effective against the particular antigenic substance. In like manner the protective principle can be admixed with other milk products such as other dairy drinks, ice-cream, sherbets, cheeses and the like.

In the treatment of both sick animals and humans the parenteral administration of gamma globulin having high antibody against a particular infection has proven to be effective. Protective principle isolated from milk from stimulated udders according to this invention is available for parenteral administration in calves to elevate the specific antibody to high levels in the blood immediately upon administration.

Isolation of Gamma Globulin with Protective Principle

Protective principle from milk containing antibody or protective principle produced by stimulation of the ungulate mammary gland may be isolated and separated for use in parenteral administration. The skim milk containing the protective principle is first separated in a conventional centrifugal cream separator to remove the fat. The pH of the milk is adjusted to about 4.6 to precipitate the casein. The skim milk may be diluted before acidification if desired. The casein is removed by sedimentation, filtering, or centrifugation.

The filtrate is adjusted to an ionic strength of about .40 to .45 and is cooled to about -5 degrees C. Ethanol is added at this temperature to make up about 25% by volume. The gamma globulin precipitates and may be removed by centrifugation, sedimentation or filtration at about -5 degrees C.

The crude gamma globulin containing the protective principle is purified by redispersing it in an aqueous salt solution and reprecipitating with alcohol at -5 degrees C. After purification the gamma globulin is freeze dried under vacuum at about -5 degrees C. The freeze drying is greatly facilitated by washing the gamma globulin with large quantities of alcohol to remove the water.

Example XX

The preparation and isolation of the active fraction containing the protective principle is illustrated as follows: A pregnant cow was first infused with *Salmonella pullorum* about 5 weeks prior to parturition. Booster doses were administered weekly until the calf was born. The colostrum milk titered 1:10, 000. Two gallons of this milk was centrifuged to remove the fat. The milk was then diluted four times by volume and the pH was lowered to 4.5 using 1 N solution of hydrochloric acid. The casein precipitated and was removed. The filtrate was adjusted to pH 6.8 with 1 N solution of sodium hydroxide. It was placed in a freezer at -5 degrees C. to stand for 2 hours for cooling. Absolute ethanol, also at -5 degrees C., was added in an amount equal to 25% by volume. This mixture stood for 8 hours and was centrifuged at -5 degrees C. The precipitated active fraction was thus concentrated and removed. It was dissolved with a small volume of water at -5 degrees C. and put in a lyophilizer flask and lyophilized at -79 degrees C. for 8 hours. The active fraction was thus transformed to a dry white powder.

It is apparent that many modifications and variations of this invention as hereinbefore set forth may be made without departing from the spirit and scope thereof. The specific embodiments described are given by way of example only and the invention is limited only by the terms of the appended claims.

The embodiments of the invention in which an exclusive property or privilege is claimed, are defined as follows:

1. The method of producing antibodies in therapeutically significant concentrations for use in animals, including man; said method comprising the steps of infusing a preselected antigen into the udder of an ungulate through teat canal and subsequent to parturition, milking said ungulate.

2. The method of producing antibodies in therapeutically significant concentrations for use in animals, including man; said method comprising the steps of infusing a preselected disease-producing antigen into the udder of an ungulate through teat canal during the pre-parturition period of said ungulate and subsequent to parturition, milking said ungulate.

3. The method of producing antibodies in therapeutically significant concentrations for use in animals, including man; said method comprising the steps of infusing a plurality of preselected disease-producing antigens into the udder of an ungulate during the preparturition period of said ungulate and subsequently milking said ungulate, collecting the milk and preparing the collected milk for sale as an antibody concentrate of pre-determined types and characteristics.

4. The method according to claim 3, wherein the infusion is repeated during the non-lactating period.

5. The method according to claim 3, wherein the antigen is a bacteria.

6. The method according to claim 3, wherein the antigen is a virus.

7. The method according to claim 3, wherein the antigen is a spermatozoa.

8. A composition comprising milk enriched with antibodies to a preselected antigen as a result of the antigen having been infused into the udder of an ungulate through teat canals, said composition being adapted for ingestion by animal, including man, and being characterized by its concentration of said antibodies, said concentration being sufficient to effect an absorption of a therapeutically significant portion of said antibodies into the blood stream of said animal upon ingestion.

9. The composition according to claim 8, wherein the antigen is a bacteria.

10. The composition according to claim 8, wherein the antigen is a virus.

11. The composition according to claim 8, wherein the anti-

gen is an allergen.

12. A method of producing gamma globulin enriched with specific protective against an antigenic substance which comprises the steps of injecting the antigenic material into mammary gland of an ungulate animal, recovering the milk from said animal, separating the milk to remove the fat, precipitating and removing the casein, adjusting the ionic strength to from about 0.40 to 0.45, cooling to about -5 degrees C. and adding alcohol to precipitate the gamma globulin.

13. A method of producing gamma globulin enriched with specific protective principle against an antigenic substance which comprises the steps of injecting the antigenic material into the udder of a cow about 2 to 8 weeks before parturition and repeating the injection at spaced intervals, milking the cow after parturition, separating the milk to remove the fat, acidifying the skim milk to precipitate the casein, adjusting the ionic strength to from about .40 to .45, cooling to about -5 degrees C., adding alcohol at this temperature to about 25% by volume to precipitate the gamma globulin and removing and separating the gamma globulin.

14. Gamma globulin enriched with specific protective principle against an antigenic substance produced according to the method of claim 12.

Immune Milk Treatment of Rheumatoid Arthritis -- Review

W. E. Peterson Research Institute, St. Paul, Minnesota

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HISTORY One of the most important discoveries of the 20th Century is the relationship of bacterial infection and hyperimmunization to rheumatoid arthritis.

In the 1930's and 1940's Edward C. Rosenow (10), Mayo Clinic, and M. Wetherby (15), University of Minnesota Medical School, conducted experiments which led to the isolation of *Streptococcus* and *Staphylococcus* from patients with rheumatoid arthritis.

In the very recent period there has been researched by Mayo staff members contributing to our knowledge of bacteria and arthritis (13). Also, during this period, Sir William E. Petersen et al. (8, 12) did research at the University of Minnesota concerning bacterial immunization of animals for the production of antiserum for disease control. Particularly important were the studies dealing with the immunization of the bovine and the finding that milk serum would give relief to patients with rheumatoid arthritis.

The importance of the agents in causing the individual to develop immunity and the specific hypersensitivity of the individual are widely recognized. Luther L. Terry (14), Surgeon General, Public Health Director, stated the importance of the immunological aspects to the prevention and cure of rheumatoid arthritis at a meeting of the Committee of Appropriations of the House of Representatives.

BASIC PRINCIPLES Milk serum from hyperimmunized cows contains high levels of antibodies. When a person ingests these antibodies, the univalent (small blocking) antibodies protect the individual. The person receives help in tow ways: (i) the antibodies are carried to the foci of infection to assist the body defense, and (ii) the antibodies move to the site of the reactive surfaces where the antigen-antibody complexes are and result in a neutralization-type action.

We believe that arthritis is the result of deposition of an insoluble antigen-antibody complex of the bacteria in the connective tissues of the patient, such as reported by Felton (5), with the accompanying development of collagen. The foci of infection provoke a low-intensity allergic inflammation which is the essential nature of the arthritis. These sites of allergic reactions are generally the joints and articulate surfaces, just as the sites for allergic reaction against inhalant antigens (pollens) tend to be centralized in the nasal and upper respiratory tract.

The importance of bacteria to hypersensitization of rheumatoid arthritis is based on extensive studies (2). Dawson (4) has shown that serum from patients with rheumatoid arthritis agglutinates and precipitates hemolytic streptococci. Sixty-seven % of the cases of rheumatoid arthritis gave agglutination, whereas other workers showed positive results in 84% of the cases. Paul Holbrook (6, p. 23), Tucson, Arthritis Clinic, says, "Occasionally, rheumatoid arthritis of acute onset cannot immediately be differentiated with certainty from rheumatic fever." It is generally accepted that the hemolytic streptococci, Group A, are responsible for rheumatic fever.

Streptococcus viridins has been isolated from the foci of infection in many cases of arthritis (9, 15). Staphylococci were isolated from patients and are thought to be a primary cause of arthritis as cited by Crowe (3). *Diplococcus pneumoniae* has been recognized as a causative agent since reported in 1914 (13).

The antigen used in the hyperimmunization of the cows is based upon the importance of these agents. The antigen is a suspension of killed organisms in a physiological saline solution. Each cubic centimeter contains *Staphylococcus aureus*, 4,000 million; *Streptococcus viridins*, 4,000 million; *Streptococcus hemolyticus*, Group A, Types 1, 3, 4, 5, 6, 12, 13, 16, 49, 4,000 million. This antigen is specifically compounded for use in the continental United States by the North American Antigen Company, St. Paul, Minnesota.

The absorption of immune bodies (gamma globulin) through the intestinal tract of adult humans, noted from milk by Klemperer (7) and from serum by Burrows and Havens (1), has been substantiated by Petersen and Campbell (8) and used as a means of treatment of disease as reported by Raabe (9).

SPECIFIC CASE STUDIES. Two cases in the early experimental work supervised by B. Campbell, University of Minnesota Medical School, will illustrate some of the findings. The cows producing this milk were hyperimmunized by the author.

Case 1. The patient being observed was a female, 56 years of age, who was diagnosed as having rheumatoid arthritis in the hands and wrists. She was using salicylate for pain relief. The right wrist was so weakened that she could no longer turn a door knob, nor could she wash dishes. She began drinking the milk on 5 September 1955 and within 4 days had partial remission. Within 7 days she had complete remission but continued on the milk for 2 months. Her hands and wrists strengthened, and as of 1963 the remission has been permanent.

Case II. The subject, a female of 53 years, had arthritis generally dispersed in the lower back and legs, particularly in the knees. She started drinking milk at the rate of 1 quart (1 pint at a time) / day on 26 November 1957. On 2 December she noticed that her pain was disappearing, and it required 27 days for full pain remission. She continued drinking the milk until 23 December 1957. On the following 5 January she noticed that the symptoms were returning, and by 13 January her condition was that of the beginning of the experiments. (This may indicate that there was only sufficient immunity to overwhelm temporarily the reactive surfaces.) Beginning 6 April 1958, milk was again taken at the same rate. First she noticed relief of pain and by 11 April there was complete relief of symptoms. The ingestion of milk was continued until 25 June. There has been no return of arthritis.

LARGE SCALE EXPERIMENTS Our findings from analyzing the records of persons drinking 1 quart of immune milk / day indi-

cate that over 80% of those persons having joint involvement, diagnosed by medical doctors as rheumatoid arthritis, benefited. However, the percentage of those who improved decreased to below 60% when persons with all types of joint involvement were considered.

Cyril M. Smith (11), Minnesota physician, conducted a large sample survey of 199 persons who used immune milk in the treatment of rheumatoid arthritis symptoms. Smith reported that immune milk was successful in 56.8% of cases reported. This improvement occurred within 3 months. The greatest improvement was noted between the second and fourth weeks. However, in some cases it required more than 6 weeks before a marked improvement was noticed.

The tabulation of results revealed that the immune milk was more frequently successful in those cases that had responded to aspirin prior to taking the milk than in those that had not.

Twenty-three % of 113 persons who found relief from symptoms while taking milk experienced an increase in pain prior to there improvement. The great majority of the persons who experienced this pain made marked improvement.

Smith (11) found that "Steady consumption of the milk as directed results in relief with fewer quarts of milk than if intake is not steady."

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A History of the Use of Immune Milk in the Treatment of Fall Pollenosis

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This presentation includes basic principles, a history of specific cases, controlled studies, and current research. The basic principle is that pollen and pollen extract of the common fall pollens, when injected into the cow, produce antibodies that when consumed by individuals produce immunity. This does not happen spontaneously; therefore, the antibodies must be consumed with regularity before protection is obtained.

The first studies on the use of immune milk in the treatment of fall pollenosis were done in 1955 with four persons who were primarily allergic to ragweeds (*Ambrosia trifida* and *Ambrosia elatior*). Sensitivity was determined by skin testing and time of year when allergies occurred. In the skin testing method, the patient scratched his skin and the author randomly applied pollen and pollen extract. The pollen and pollen extract were prepared daily by adding pollen to physiological saline.

The antigen used in the intramammary infusion of the cows was composed of 200mg of ragweed pollen in 20ml of physiological saline. The cows were infused at weekly intervals during the prepartum period; only the milk produced during the first 5 days was utilized. All four persons reported relief -- three reported complete freedom from symptoms. The individuals were also skin tested and all four were completely negative. These four persons reported an identical pattern in the disappearance of symptoms: first, the cessation of respiratory tract congestion, second, the coryza of the nose, and last, the conjunctiveness (reddening) of the eyes. It required 9 to 10 days for all symptoms to disappear completely; however, 21 days elapsed from start of consuming the milk until all response to the skin test was eliminated and a complete negative reading was obtained.

In 1956, three experiments were made: (i) relief of skin sensitive reaction, (ii) allergy occurring in the fall to other than giant ragweed, and (iii) a control experiment on the efficiency of immune milk in relief of fall pollenosis. The first study was begun in the spring, dealing with changes in skin sensitivity in six persons allergic to fall pollens. A representative case study is that of a 25-year-old male veterinary student who had a history of severe fall pollenosis since childhood:

18 April (prior to drinking immune milk) ---
Extremely sensitive to skin test (a 20-mm wheal, large pseudopodium); control test negative. Time from challenge to maximum skin reaction 13 min.

25 April (after drinking immune milk for 1 week) ---
Still extremely sensitive with wheal; control test negative. Time for maximum skin reaction 13 mim. Continued milk.

2 May (2 weeks later) ---
Slight reaction to skin test; control test negative. Time for maximum skin reaction 13 min. Continued milk.

9 May (3 weeks later) ---
No reaction to skin test and free of irritation; control test negative. Test and control test area had same characteristics. Stopped drinking milk.

23 May (5 weeks later) ---
No reaction; control test negative.

6 June (7 weeks later) ---
Slight to moderate reaction; control test negative. Time for maximum skin reaction 13 min.

14 June (8 weeks later) ---
Sensitive with wheal but no pseudopodium reaction; however, reaction not as great as on 18 April; control test negative. Time for maximum 13 min.

The five other persons in the test responded in a similar manner.

The second study was in the fall of 1956 and it dealt with allergic response to fall pollens other than ragweed. Experimental work in the previous years had shown that many persons who believed they were allergic only to ragweed did not get complete remission when drinking immune milk when the cows were treated only with ragweed. Therefore, the pollens and extracts of giant ragweed, small ragweed, lambsquarters (*Chenopodium album*), and red root pigweed (*Amaranthus retroflexus*) were used. Sixteen

people, ranging from a 10-year-old girl to a 50-year-old man, consumed the milk. The results were as follows: 10 (or 63%) reported complete freedom from symptoms -- including coyza, conjunctiveness, and edema in the afflicted area; six persons reported partial freedom from symptoms, and one person noticed no benefit from the milk. All people in the trial drank only *1* pint of milk per day. However, four of the six people who had partial freedom reported almost complete freedom when they consumed 2 pints per day -- the recommended dosage is 2 pints per day, one in the morning when arising and one between meals or prior to retiring in the evening.

The major study in 1956 was a fully controlled experiment to indicate the efficiency of immune milk in relief of symptoms during August, September, and October. This experiment was conducted by Jacob Blumenthal, M.D., Director of the Allergy Clinic, University of Minnesota, and used as a dried skim milk powder produced by the author. The milk was the first 10 days of milk produced by the hyperimmunized cows treated with pollen and pollen extracts of giant and small ragweed, lambsquarters, and pigweed. The milk powder used as a control was obtained from Twin City Milk Producers Association, St. Paul, and was a low heat Grade A product. Both powders were packed in identical medical containers. The patients were not told which milk they were given nor did the clinician who examined the patients know which milk they were taking. The design of the experiment was to have 36 persons consume each milk. The results of this preliminary study were not fully presented by Blumenthal prior to his death. The results are those reported by his colleagues.

The number of persons receiving relief, as cited by C. J. Watson, M. D., Professor of Medicine, University of Minnesota, in reporting on Blumenthal's study, was stated as follows: ". . . of 36 individuals using antibody milk, 15 apparently had good results, 9 had fair results, and in 12 there was no change." Thus, 66% reported complete or partial relief when drinking immune milk.

An analysis by the Statistical Division, School of Public Health, University of Minnesota, of the response in the two groups showed a four standard deviation difference in favor of the immune milk over the control milk. I believe only three persons reported improvement on the control milk.

In 1957-58, a new sequence of infusion was developed, that of first giving prepartum infusion at weekly intervals followed by infusion at weekly intervals during the milking phase. Also studied was the relationship of day of infusion to efficiency of the milk. Since the cows were infused weekly (Monday morning), the milk was kept separate for Monday-Tuesday; Wednesday, Thursday, Friday; and Saturday-Sunday. These three milks were compared. The results, as reported by the persons who drank the milk, were no observable difference.

In 1959, studies were made with those individuals who did not respond to immune milk as then produced. The findings were as follows: when pollen and pollen extracts of mugwort (*Artemisia vulgaris*), wormwood (*Artemisia annus*), Russian thistle (*Salsola pestifer*), and late summer grasses were included in the antigen used in intramammary infusion, many refractory persons received freedom from symptoms. Also in 1959, clinical studies were conducted by Clarence Siegel, M. S., St. Paul, Minn., using milk produced by cows receiving a broad pollen base --- the cows were hyperimmunized during the postpartum period and this milk was used. The hyperimmune milk was frozen in pint containers. A total of 30 persons drinking the milk reported that relief of symptoms required from 10 to 15 days.

In 1961 and 1962, a study was made of time of parturition as it affected difficulties, at parturition, health of young, ease of removal of fetal membranes, and milk production. In previous years it had been observed that cows that received hyperimmunization of pollen and extracts during these postpartum period and calved (parturition) during the latter part of August or September had severe mastitis and produced very little milk. This experiment confirmed these results. Those hyperimmuned cows that calved during that period of high pollen did not produce the expected quantity of milk, but other factors were normal. The three cows that calved during the latter part of August had severe mastitis and after 7 days no longer produced milk. Cows that had similar treatment but calved in June produced at 40 to 60 pounds of milk per day. Our current method is to produce the fall pollen milk prior to the pollen season.

Also in 1962 a two-phase study was made of the effectiveness of immune milk produced from a broad-spectrum pollen antigen derived from the following pollens:

1. Giant ragweed *(Ambrosia trifida)*
2. Small ragweed *(Ambrosia elatior)*
3. Pigweed, red root *(Amaranthus retroflexus)*
4. Lambsquarters *(Chenopodium album)*
5. Mugwort *(Artemisia vulgaris)*
6. Wormwood, annual *(Artemisia annus)*
7. Russian thistle *(Salsola pestifer)*

The ragweed fractions (1 and 2 above) comprised 60% of the pollens.

The first phase was to have each person answer a short questionnaire giving his observations each time he received a new supply of immune milk. This was every 2 weeks during the fall months. Over 95% of the people reported that immune milk was beneficial.

The second phase was a very complete questionnaire which was mailed to 56 people who had taken the milk this year. These people were chosen at random. Sixty-four % returned the questionnaire. Of these, 75% reported complete relief, 11% partial relief, and 14% little or no relief. An interesting comment was that 23% of those who received complete freedom from all symptoms reported that they took low levels of antihistamines. These people reported partial relief with milk alone or with milk and other drugs but complete relief with immune milk and less than recommended levels of antihistamines.

Current research has been along two lines: (i) a study of mold allergies, and (ii) the use of the isolated gamma globulin from immune milk. Many people have reported increased sensitivity to molds during the fall pollen season. Recently published work shows that the incidence of mold sensitivity, as determined by skin tests, among persons with allergies was extremely high and that treatment of mold allergies in addition to pollen allergies is important. The preparation of antigens for intramammary infusion has been the addition of 1cc of a 1:10 mold solution of five common molds --- *Alternaria, Hormodendrum, Helminthosporium, Aspergillus*, and *Penicillium*. Insufficient data have been obtained to make a determination of the use of a multiple-species mold extract.

Present studies with the isolated gamma globulins are with the ammonium sulfate-precipitated gamma globulin from immune milk. The recommended dosage is 200mg of gamma globulin in a standard No. 0 gelatin capsule (nonenteric coated) taken with a glass of water when first arising in the morning. Present indications are that capsules may be more effective than taking immune milk.

The future plans are for the purification and separation of the gamma globulin into smaller molecular weight fractions which can be utilized by the medical doctor as injections. Present experiments with animals are most promising for passive immunization by way of injections.

Immune Milk in the treatment of Poison Ivy

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Immune milk, as defined in this paper, is the milk produced after the mammary gland has been hypersensitized by Ivyol, a commercial preparation extract of *Rhus toxicodendron* which is a 1:1,000 extract of poison ivy and poison oak in olive oil. It is prepared by Merck, Sharp and Dohme, Division of Merck and Co. Inc., Philadelphia. The milk used in these cases was obtained from normal, healthy cows in their third and fourth lactation that were without histories of severe mastitis. All of the animals were housed under standard, conventional dairy management practices and fed good quality alfalfa hay plus grain.

The immune milk was prepared by introduction of 1ml of Ivyol into each quarter via a teat cannula. The hyperimmunization procedure was started 21 days prior to expected parturition and repeated each 7 days until parturition; consequently, the last injection was sometimes less than 7 days before parturition. After parturition, the hyperimmunization sequence was continued, the mammary gland being infused every 7 days. There was no evidence that the immunization caused inflammation of the mammary gland before or after parturition; however, there were elevated temperatures about 6 hr after infusion. These temperature elevations were transitory.

All colostrum and all other milk was saved during the experiment. The milk was immediately frozen in half-gallon paper containers and stored at subzero temperatures.

At the time of use, the milk was thawed and stored at normal refrigerator temperature until consumed. Sometimes the milk separated into solids and sera. When destabilization occurred, the patient either stirred the milk into a suspension or ran it through a hand homogenizer. In no case was there any refusal to drink the milk.

The following report deals with the use of the above milk in the treatment of three severe cases of poison ivy. In each case the patient had been refractory to standard medical treatment and the milk was used as a last resort.

Patient No. 1 --- This patient was a male college student who was afflicted by the poison ivy syndrome over most of his body. He contracted the poison ivy from the vapor and smoke of a fire. Apparently the volatile material had passed through his clothing. The affliction was severe enough to require hospitalization; the medication was 1 pint of immune milk consumed twice daily. Within 24 hr after the first quart of milk, the itching had subsided. After 72 hr he returned home and healing continued at a normal rate. A total of 6 quarts of milk was consumed.

Patient No. 2 --- This patient was a teen-age girl who had a history of becoming affected by poison ivy. Each summer, apparently because of her sensitivity, she easily became affected, and each summer this condition continued until autumn. When this patient was first observed, she complained of having had the irritation for 3 weeks. Her ankles and legs were markedly swollen. In addition to the swelling there was a great number of broken blisters that had become open sores.

She consumed 1 quart of milk daily for 1 week. At the end of the first day the itching had abated. Three days later, the open sores were scabbing over and healing was progressing rapidly. At the end of 1 week this patient was over the poison ivy attack. There was no recurrence during the summer.

Patient No. 3 --- This patient was a teen-age girl who was severely afflicted on her left arm and upper thorax. The contact with poison ivy was made while sunbathing. Many large blisters had formed, and scratching had caused many to break and produce scabs. She was in great pain. After normal treatment failed to reduce the pain and irritation, she was given 1 quart of milk daily for 6 days. By the end of the 24 hr the itching had abated and healing proceeded uneventfully.

In each case, immune milk was given as a last resort as the patients had been given various types of medication prior to drinking the milk.

In each case the severity was extreme; the response was most dramatic and conclusive. The cessation of itching and the stopping of blisters in addition to rapid healing are strong evidence that the property for arresting the causative agent of poison ivy is present in this immune milk.

UNITED STATES PATENT OFFICE 3,376,198
Patented Apr. 2, 1968
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METHOD OF PRODUCING ANTIBODIES IN MILK

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No Drawing, Continuation-in-part of application Ser. No 789,502, Jan. 28, 1959, which is a continuation-in-part of application Ser. No. 500,038, Apr. 7, 1955. This application July 21, 1965, Ser. No. 473,833.

14 Claims. (Cl. 167-78)

This invention relates to the production in the mammary glands of ungulates, of high specific antibody or protective principle effective against a wide range of antigens and useful for the precipitation of antigens in purification or analysis of protein compositions in the manner of an antiserum. More particularly, the invention concerns the production of milk in its natural state fortified with naturally occurring antibodies to preselected antigens. This application is a continuation-in-part of the application Ser. No. 789,502, filed Jan. 28, 1959, as a continuation-in-part of an earlier application Ser. No. 500,038, filed April 7, 1955, both now abandoned.

The term "milk in its natural state," as used herein, means milk or colostrum in the form in which it comes from the udder of a cow or other ungulate and prior to processing of any kind.

Naturlly occurring antibodies refers to antibodies occurring in milk as a result of the natural metabolic processes in the milk as a result of the natural metabolic processes of the cow, even though subject to external influences. It does not refer to antibodies added to milk subsequent to milking. The term "antigen" refers to a material antigenic to the treated ungulate.

In an abandoned patent application, Ser. No. 628,987, filed Nov. 15, 1945, an abstract of which was published in the U.S. Patent Office Gazette on Dec. 5, 1950, the applicant, Holm, suggests the possibility of treating disease by the ingestion of milk fortified with naturally occurring antibodies where said antibodies have been induced by actively immunizing a cow with a preselected antigen. However, Holm failed to secure a significant number of antibodies because he followed the usual immunization procedure of intramuscular and intravenous injections of antigen, hoping that the milk would absorb a significant proportion of these antibodies from the blood of the animal. This type of injection does not yield a therapeutically significant concentration of antibodies in milk in its natural state.

In August 1951, Porter, working under our direction, published his doctoral thesis at the University of Minnesota (Biological Abstracts 1953, p. 951, par. 10, 185), in which he suggested the pos-

sibility of manufacturing antibodies in the cow's udder by infusion of antigen into the udder of a lactating cow. This was a revolutionary departure from prior thinking for although it was known that relatively minor quantities of antibodies could enter the milk from the blood stream and that antigens could exercise their effects via the udder, ti was not thought that the udder itself could play a significant manufacturing role in the immunity scheme.

Porter therefore suggests the infusion of selected antigens into the cow's udder during the lactation period with the hope

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of increasing the effective concentration of antibody in milk in its natural state to effective economic levels; but Porter's proposal, like Holm's procedure, was incapable of accomplishing the desired results.

In addition to the problem of securing an increase in numbers of antibodies in milk in its natural state, there is also the extremely important matter of economic feasibility in relation to procedural requirements. Although it is possible with the methods of Holm and Porter to produce antibody-containing milk, and also possible to employ well known concentration procedures to reach some effective level of therapeutic concentration, this would be economically unfeasible for the reason that the high cost of producing such antibodies precludes any widespread use.

The ultimate problem which faced us was to discover and provide a method of antibody production in the cow's udder which will yield milk in its natural state with the required concentration of antibodies, without requiring further concentrating or processing of the milk. By this invention we have solved that problem.

A principle object of this invention thus is to provide a method of producing milk inits natural state fortified with a concentration of naturally occurring antibodies not attained heretofore.

It is also an object of this invention to provide a compostion comprising milk in its natural state fortified with natrually occurring antibodies therapeutically significant concentrations.

Another major object of this invention is to provide a high concentration of antibodies on an economically feasible basis for use in precipitating proteins from protein compositions for purposes of purification, analysis and the like.

With the above and other objects in view which will appear as the description proceeds, this invention resides in the novel procedures and methods substantially as hereinafter described and more particularly defined by appended claims, it being understood that such changes in the precise embodiment of the hereindisclosed invention may be made as come within the scope of the claims.

In accordance with the present invention, high concentrations of specific antibody in the milk of ungulates (particularly cows, goats, sheep, etc.) are produced against any antigen by introducing such antigen into the udder of the animal during the pre-parturition period that is, during pregnancy. This may be done through the teat canals, in which event the introduction is ordinarily referred to as infusion, or the antigen may be injected hypodermically through the wall of the udder close to the base of each teat, or wherever the injected antigen is sure to reach the cistern of the udder. To product the maxium concentration of antibodies, the antigen may be introduced into the udder at about weekly intervals prior to parturition. Subsequent to parturition, declining antibody concentrations can be increased by periodically introducing booster shots of the selected antigen into the udder during the lactating period.

Although the amounts of antigen introduced, the frequency (time interval), and the number of booster doses may vary widely, the highest antibody response in milk results from the introduction of a plurality of doses of increasing amounts into the udder of an animal in its preparturition period over a period of several weeks. For example, the initial injections can be initiated from about two to eight weeks before partur-

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ition.

The size and concentration of the antigen doses are not critical but are selected for convenience. It has been found that increasing or decreasing the size of the antigen injection does not produce a corresponding increase or decrease in the protective principle titer of the resulting milk.

Booster shots, when given to the lactating cow, may likewise be spaced to suit the convenience of the operator, except that they should be administered frequently enough that an antiphylactic reaction does not occur. For most species that time is less than about ten to fourteen days. To avoid local irritation and congestion, it is usually preferred that booster shots not be given more frequently than every other day.

The antigenic substances are suspended in liquid medium for infusion or injection, such as, for example, a sterile physiological saline solution. The booster shots which are administered to the lactating cow may be given intravenously, intramuscularly, subcutaneously, or may be made into the duct system of the udder through the teat meatus and into the gland cistern. The udder may, if desired, be massaged for better penetration of the antigen into the duct system of the udder.

The antigenic substances which are employed in the practice of this invention for the production of protective principles include bacteria, viruses, proteins, animal tissue, plant tissue, spermatosoa, rickettsia, metazon parasites, mycotic molds, fungi, pollens, dust and similar substances which are antigenic to the treated ungulate. Exemplary antigens include: bacterial--*Salmonella pullorum, Salmonella typhi, Salmonella paratyphi, Staphylococcus aureus, Stap hylococcus albus, Staphylococcus pyogenes,* pneumococcus, streptococci, and the like; viral--influenza Type A, fowl pox, turkey pox, herpes simplex and the like; protein--egg albumin and the like; tissue--blood and sperm. The expressions "antigenic substances" and "antigenic material" means anything which stimulates antibody production and include materials which are antigenic in and of themselves to the ungulate and also non-antigenic materials which act as antigens in the presence of adjuvants. Antigenic disease organisms are specifically include within these expressions.

EXAMPLE 1

The experimental subject was a Jersey cow, five weeks before parturition. The antigen was dead *Salmonella pullorum*. The initial dose of antigen was introduced into the udder through teat canals, 1ml. of antigen per quarter, and each containing approximately 5 billion organisms. One week later, a repeat dose of 1 ml. antigen per quarter but containing 10 billion organisms was introduced intothe udder. Subsequent doses of 1 ml. per quarter containing increasingly larger concentrations of the antigenic material, about 20, 30 and 40 billion dead organisms, respectively, were injected at one week intervals. Milk following parturition, from agglutinated the antigen at more than 100,000 dilutions , a dilution greatly in excess of that produced by the methods of Porter or Holm.

The antibody or protective principle in the milk decreased rapidly following parturition, from agglutination at more than 100,000 dilutions in four weeks. The level of the protective principle was then brought up and maintained by systemic

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administration of antigen.

EXAMPLE 2

The procedure of Example 1 was repeated on a different cow, the only difference being that the doses of antigen both for the initial introduction and the repeat doses were one-tenth as concen-

trated as those used in Example 1. The resulting milk was high in protective principle, there being no apparent difference from the milk of the first example.

EXAMPLE 3

To show the production of protective principle against a specific combination of antigenic substances, a mixture of approximately equal numbers of Pneumococcus, type 1, Pneumococcus, type 2; *Salmonella typhi, Salmonella paratyphi* and *Staphylococcus albus,* was introduced into the udder of a cow two weeks before calving. A similar mixture was introduced one week later. The milk after calving showed a strong reaction for antibody against all of the injected species.

EXAMPLE 4

Production of protective principle in goats was carried on by giving daily infusions of 1 ml. of a suspension of *Salmonella pullorum* via the teat canals to a pregnant goat. The daily infusions were given over a period of more than four months prior to parturition. Results comparable to Example 1 were obtained.

EXAMPLE 5

A Jersey cow just starting to "udder down" was given an initial dose of M-VI *Salmonella typhimurium* containing 5 million dead organisms per ml. by hypodermically injecting 5 ml. thereof into each quarter. The injections were made with a stainless steel 18 gauge hypodermic needle three and one-half inches long, the needle being inserted into the udder close to the base of each teat at such an angle that the antigen, which was released when the mouth of the needle was in the cistern, was dispensed in the area directly above the teat.

The same dose was injected into the udder in the same way, both one week and two weeks after the initial injection; and the day after the third injection, the cow freshened, that is, had her calf. Six days after she freshened, the same doses of *Salmonella typhimurium* was again hypodermically injected into each quarter of the udder. The milk taken from the cow at that time was checked and found to have a high concentration of antibody and good titer. Her milk production was average for a cow of her size and type.

Where the introduction of the antigen into the udder is hypodermic injection, as in Example 5, the specific point at which the needle is inserted is not too important as long as the antigen reaches the cister of the udder in the form in which it is injected.

The antibody or protective principle produced in accordance with our invention may be preserved, if desired, in pasturized milk, condensed milk, dried milk and in gamma globulin isolated from the milk. Pasteurization has no

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adverse effect upon the protective principle.

The milk containing protective principle may be freeze-dried or may be condensed under careful temperature control. Dried milk containing the antibody or protective principle is preferably prepared from the non-condensed product. However, the condensed milk may be used if at first condensed carefully at low temperatures to avoid destroying of the protective principle.

Drying can be also accomplished by the convential spray or roller drying processes under properly controlled conditions in order to preserve the protective principle. High temperatures per se are not detrimental to the protective principle except when sustained for a period of minutes. Thus the milk may be dried in a dryer in which temperatures of 300-400 degrees F. are achieved, if the milk is at these temperatures only for an instant.

A proliferating virus can be administered to the udder in a two-stage operation. The first inoculation can be made in a lactating cow. The second infusion is then made into a second cow in the pre-parturition period, the infusion being milk resulting from the first, with the accompanying tissue antigens diluted out. This screening procedure is illustrated by the following:

EXAMPLE 6

A cow was infused through the teat canals with Herpes simplex virus in mouse brain suspension. The cow was lactating and was regularly milked thereafter. The next day the milk showed a positive Whiteside test. On the second day following the inoculation, the milk was used for introduction into the udder of a dry cow, also through the teat canals. The result was the transfer of the virus without the mouse brain antigens. The expected antibody response to the virus occurred.

The antibody or protective principle which is the product of this invention is useful in a variety of ways. It has been discovered that the productive principle or antibody is absorbed into the system after the milk fromstimulated udders has been ingested or administered by proctocylsis. The isolated and separated protective principle may be administered orally, rectally, parenterally and topically. The protective principle is useful in the immunization and treatment of animals.

The application of the protective principle of this invention is illustrated by the following examples:

EXAMPLE 7

The protective principle against *Salmonella pullorum* was applied to fowl. The experimental subjects were six adult chickens, all negative to the Salmonella antibody test. After one feeding of the milk containing the protective principle, all of the chickens developed a strong positive reaction.

EXAMPLE 8

A further application of the protective principle of this invention was made to chickens and showed positive protection afforded by the protective agent. Twenty day old chicks were divided into an experimental group of ten and a control group of ten. The experimental chicks were fed milk ac-

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cording to this invention with antobodies against *Salmonella pullorum. Salmonella pullorum* is a chicken disease organism. The controls were fed milk with no such antibody. During the first day of the experiment, the two groups were injected intracardially with an infusion of live *Salmonella pullorum* in broth. The mortality of the controls was heavy, the fifth chick being dead in 24 hours while in the experimental group, the fifth death did not occur for 120 hours.. The general state of health of the control chicks was poor as compared with the experimental group. This is a severe test of the protective principle since the organisms were injected directly into the hearts of the experimental subjects, a mode of transmission which would never be encountered normally.

Chickens as a species are far removed from the cow, yet the protective principle produced in the cow is readily conveyed by the milk into the blood stream of the chickens by absorption through the digestive tract.

EXAMPLE 9

The protective principle was applied to bovine subjects. The subjects were two five month old calves with fully functional rumens. The calves were negative to the Salmonella antibody test. After two feedings of the milk containing *Salmonella pullorum* protective principle they developed strong positive agglutination reaction in the blood.

EXAMPLE 10

Porcine animals were also tested. The experimental subjects were two mature pigs weighing about 200 pounds each, and negative to the antibody test. After one feeding of milk containing protective principle against *Salmonella pullorum,* both pigs developed a weak reaction. After two feedings of milk they showed a strong

reaction in the blood.

Experiments with calves and pigs show that with continued ingestion of the milk containing the antibody, the levels of the protective agent continue to increase in the blood. Experiments with calves also show that the protective principle is absorbed from the rectum. The rate of absorption from the rectum is less than from the anterior part of the system. Rectal absorption may be resorted to, however, if oral administration is contraindicated. The high antibody or protective principle containing material may be applied topically (unction) in treatment of local exacerbations due to allergy.

Salmonella pullorum antigen has been used in the experimental work described in the above examples because it is relatively harmless to the experimental subject; it is readily available, easily identified and its absorption into the system of the subject can be readily traced by the agglutination test. It is to be understood, however, that this specific bacterial antigen is used for illustrative purposes only and the invention is not so limited.

With the discovery that the protective principle or antibody in sufficiently high concentrations can be absorbed from the digestive tract and that it is possible to produce specific antibody to antigens by proper treatment of ungulates to stimulate such antibody or protective agent development, avenues are open for a new approach to the prevention and treatment of disease in animals. The initial step in this direction is the production of specific protective principle against a mixture of all known antigens for animals or the production of

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one specific protective principle such as antibody against a specific antigen.

Since the mammary gland of the cow will produce specific antibody against any of the antigens named herein, milk may be prepared with protective principle useful against infectous disease organisms and other antigens in animals. Specially prepared milk containing specific antibodies against specific, although rare diseases, and other specific antigen induced conditions may be produced. For example, protection from ragweed pollen is offered by consumption of milk with a high protective principle against ragweed pollen. This latter example, the production of a protective principle against an allergen is completely novel. The prior workers, including Holm and Porter, had no idea that such a result could be achieved.

An important application of the protective principle of this invention in the field of animal treatment is furnishing protective colostrum for calves. At the present time it has been estimated that some 20% of all ca;ves born alive die within the first few weeks of life. Death is caused principlaay by infectious organisms against which antibodies may be developed. Mixed antigens of all of the common infectious diseases that kill calves are prepared and injected appropriately into the udders of cows in their pre-parturition period. The colostrum for such stimulated udders may be used as feed directly or may be dried, packaged and made available to feed calves immediately after birth to give calves the necessary level of antibodies to carry them through the critical part of their life.

For administration of the protective principle of this invention to animals, a preferred method is by incorporation into milk and other dairy products. While prior methods were unable to produce a therapeutically significant concentration of antibodies in milk in its natural state, the present method yields an over abundance which permits of its dilution with milk. Since milk as produced by the method of our invention agglutinates at dilutions as great as 100,000, the original milk containing the protective agent can be greatly diluted with non-protective milk and distributed and fed in this form. Ordinarily, milk may thus be given a high protective level against specific antigenic materials. The amount of dilution is dependent upon the titer of the antibody enriched milk and the required level of antibodies needed for effectively combating the specific antigen and the like. As an example, a gallon of the original high-titer (say, 1:100,000) milk from a cow treated to produce protective principle against any particular antigen, may be admixed with nine gallons of ordinary non-protective whole milk to produce ten gallons of milk sufficiently hihg titer (1:100,000) to be effective against the particular antigenic substance.

What is claimed as our invention is:

1. The method of producing antibodies in therapeutically significant concentrations in milk in its natural state, comprising the steps of:

(A) introducing a plurality of preselected antigens in a non-pathogenic condition into the udder of a pregnant ungulate through a teat canal, and

(B) subsequent to parturition, milking said ungu late.

2. The method of producing antibodies in therapeutically significant concentrations in milk in its natural state, comprising the steps of:

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(A) introducing a preselected antigen in a non-pathogenic condition into the udder of a pregnant ungulate through a teat canal, and

(B) subsequent to parturition, milking said ungulate.

3. The method according to claim 2, wherein the introduction is repeated during the pre-parturition period at intervals over about two to eight weeks.

4. The method according to claim 2, wherein the introduction of said antigen into the udder of said ungulate is repeated during the lactation period of said ungulate when antibody to said antigen has substantially declined.

5. The method according to claim 2, wherein the ungulate is a cow.

6. The method according to claim 5, wherein the antigen is a bacteria.

7. The method according to claim 5, wherein the antigen is a virus.

8. The method according to claim 5, wherein the antigen is a protein.

9. The method according to claim 5, wherein the antigen is spermatozoa.

10. The method according to claim 5, wherein the antigen is a allergen.

11. The method according to claim 5, wherein the antigen is ragweed pollen.

12. The method of obtaining from an ungulate normal milk containing therapeutically significant concentrations of an antibody against a preselected antigen, without upsetting the normal milk producing function of the ungulate, which method comprises the steps of:

(A) introducing said preselected antigen in a non-pathogenic condition directly into the cistern of the ungulate's udder while the ungulate is pregnant; and

(B) subsequent to parturition and cessation of the period during which the ungulate produces colostrum, milking the ungulate.

13. The method of obtaining from an ungulate normal milk containing therapeutically sugnificnat concentrations of an

antibody against a preselected antigen without upsetting the normal milk producing function of the ungulate, which comprise the steps of:

(A) inserting the needle of a hypodermic syringe containing a quantity of said preselected antigen ina non-pathogenic condition, through the wall of a portion of the udder of the ungulate while the ungulate is pregnant, to thereby bring the discharge end of the needle into open communication with the cistern of the udder;

(B) expelling the contents of the syringe, so that said non-pathogenic antigen reaches the cistern of the udder in the form in which it is contained in the syringe; and

(C) subsequent to parturition and cessation of the period during which the ungulate produces colostrum, milking said ungulate.

14. The method of obtaining from an ungulate normal milk containing therapeutically significnat concentrations of antibody against a predetermined pathogenic organism known to affect the health of animals, which method comprises:

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(A) introducing an antigen originating from said organism, but in a non-pathogenic condition, directly into the udder of an ungulate while the ungulate is pregnant and in a manner which assures that said antigen reaches the cistern of the udder in the form in which it is introduced; and

(B) subsequent to parturition and cessation of the period during which the ungulate produces colostrum, milking the ungulate.

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Collins et al. PATENTED Sep. 6, 1983

FOOD AND THE METHOD OF EXTRACTING THE SAME FROM COLOSTRUM AND MILK

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[57] **ABSTRACT**

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This invention provides a new and useful food factor for use as a nutritional supplement for animals, which product comprises whey obtained from colostrum and milk as it comes from selected cows or other ungulates, and containing an active fraction having a molecular weight on the order of 1200 or less.

6 Claims, No Drawings

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FOOD AND THE METHOD OF EXTRACTING THE SAME FROM COLOSTRUM AND MILK

This application is a continuation-in-part of the pending application of Mary E. Collins, Ser. No. 154,502, filed May 29, 1980, now abandoned.

It is an object of this invention to produce a new and useful food product comprising whey, by a process which involves the prepartum introduction of specific antigen-like material into the udder of an ungulate to enhance to an economic level the food factor in whey.

It is another object of this invention to extract, from colostrum and milk from ungulates previously treated with a specific antigen-like material, the whey portion possessing the new food product by a process which entails passage of such whey through a sterilizing filter without denaturing the molecules contained therein.

It is another object of this invention to produce a variety of specific foods by varying the antigen-like material used to activate the udder—such as, but not limited to, pollen, bacteria, virus, mold,

allergens, blood from sick animals and sperm.

More specifically, it is a purpose of this invention to produce a food of the character described which is characterized by an active fraction having a molecular weight of less than 1200.

In one method of practicing our invention, the antigen-like material is introduced into the udder of an ungulate in an asceptic manner two or three times, at weekly intervals during the last month of gestation. This can be accomplished by using a sterile syringe and a blunt hypodermic needle, and injecting the material into the side of the udder; or the material can be introduced through the teat canal using a sterile syringe and a blunt plastic needle inserted through the orifice of the teat into the cistern.

At parturition, the ungulate is milked twice daily during the colostrum flow period, and the colostrum is collected in containers and refrigerated, allowing the fat to rise. The fat is then skimmed off. The skimmed colostrum is then frozen to allow storage thereof and to effect a separation of the suspended solids therein.

Milk produced following the colostrum is collected and has the fat removed by centrifugation, as by a cream separator. The resulting skim milk is most conveniently placed in five or ten gallon cans and frozen to effect a separation of the milk curd solids. These solids precipitate better the longer the milk is frozen. The usual freeze period can be sixty days or more. The frozen skim milk can be saved until a suitable size batch is accumulated, usually about fifty to one hundred (50-100) gallons.

The skimmed colostrum is then removed from the freezer and allowed to thaw gradually at room temperature. The clear liquid is then siphoned off from the colostrum and put in a refrigerator first vat. The remaining slurry is put into a second vat.

Next, the skim milk from the batch is removed from the freezer and allowed to thaw gradually, usually overnight at room temperature. The clear liquid is siphoned off and added to the clear liquid in the first vat containing the clear liquid from the colostrum.

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The remaining skim milk slurry is then added to the slurry from the colostrum in the second vat. The temperature of the slurry in the second vat is then raised to about 103 F. To 110 F., which temperature has been found to be best suited for coagulation of the milk curd solids by acid.

Hydrochloric acid (37% USP), diluted 1:10 with distilled water, is slowly added to the second vat while the combined slurries stirred. The acidity of the batch thus formed is then monitored and enough acid added to bring contents to the desired acidity, which is approximately 4.5 pH. The milk curds (solids) are removed by conventional filtering means so that only the whey portion remains. The whey thus separated from the slurry is then transferred to the refrigerated first vat containing the clear mixture of liquid previously siphoned off from the colostrum and milk.

A preservative such as phenol, parabens, etc., is next added to the refrigerated whey in the first vat. It will be understood, of course, that no more than the maximum allowable quantities of such preservatives are used.

The whey thus produced is further processed through an infiltration media of 0.2 micron and smaller have been successfully employed.

Ultrafiltration has been used in the industry for the concentration of protein and lactose in whey, a process in which the filtrate (permeate) is discarded. Our process distinguishes from that previously used in the industry by being the reverse thereof. We use ultra-filtration to remove the protein, globulin, large molecules and contaminates from the whey permeate, a portion of which consists of the desired specific food factors having a molecular weight of <1200, while the remainder contains other factors present in milk and colostrum as it comes from the cow.

Thus, in our process, the filtrate (permeate) is saved and the concentrate or retinate is discarded.

At this point, the filtrate (permeate) containing the desired food factors constituting our new product is further processed by asceptically bottling for direct consumption or by freeze-drying to produce a product in powder form. Ideally, heat substantially above that of the normal body temperature of an ungulate should not be applied to the product for concentration, and the product should not be allowed to reach pasteurizing temperature.

In addition to the specific food factor in the colostrum and milk of the ungulate treated in the manner aforementioned, our new food product also contains numerable factors normally present in colostrum and milk, some of which are viable and all of which are beneficial for animals. At the present time, we do not know the actual identity of our new food product, but its value has been proven by extensive and conclusive tests at the Lobund Institute of the University of Notre Dame.

A report on these tests, now believed to be available, can be found by reference to the official program and abstracts symposium entitled "Gnotobiology for the 80's: Technical and Application" published by "The Association for Gnotobiotics" at their 18th annual meeting held July 10-13, 1980 at the Whitehall Hotel, Houston, Tex. That symposium was hosted by the University of Texas System Cancer Center M.D. Anderson Hospital & Tumor Institute, Texas Medical Center, Houston, Tex. 77030, and the program lists the following abstract:

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20. Anticaries Effect on Colostrum Whey from Cows Treated Prepartum with a *Streptococcus mutons* Bacteria via Intramammary Infusion. Morris Wagner, University of Notre Dame, Notre Dame, Ind.

However, it has been determined that the term "specific unknown food factor", as used herein, designates a food factor having a molecular weight of less than 1200. To achieve the desired economic level of this unknown food factor in the colostrum and milk of an ungulate, it is essential to introduce pre-partum into the udder of the ungulate, a specific antigen-like material. Such antigen-like material can comprise (for instance) pollen, bacteria, virus, mold, allergens, blood from sick animals, sperm and toxins.

The presence and amount of this specific unknown food factor in our product has been established by the use of mouse protection studies at the WARF Institute of the University of Wisconsin. The method of measurement—namely, "mouse unit"—is also that which has been established by WARF.

A mouse unit is the minimum amount of our food product obtained from a specific batch, required to protect for a predetermined time a mouse that has been challenged with a lethal dose of the same antigen-like material introduced pre-partum into the udder of the donor ungulate used in the production of said batch. The accepted definition of a mouse unit is contained in the book entitled "Chemistry and Physiology of the Vitamins" by H.R. Rosenberg SC. D., revised reprint 1945: Interscience Publishers Inc. N.Y., N.Y. Page 24.

We have established that if a mouse unit is 1cc of our food product:

(A) 1cc of our product reduced to a powder by freeze drying constitutes a mouse unit; and

(B) 1cc of our product with all molecules over 1200 M.W. removed also constitutes a mouse unit.

In a more general sense, this invention can be said to reside in introducing pre-partum into the udder of an ungulate a specific antigen-like material, collecting the colostrum and milk after par-

turition, processing it by extracting the whey therefrom, and filtering the whey through a filter having a pore size preferably not greater than 0.2 microns. The final filtrate contains the desired unknown food factor, along with all factors in whey processed from colostrum and milk as it comes from the treated ungulate.

In addition to the unknown food factor, enhanced to an economic level by the pre-partum introduction of a specific antigen-like material into the udder of an ungulate, our new food product contains other beneficial factors on the order of B Lysin, Conglutinin, Interferon,Lactoferrin, Lactoperoxidase, B Lymphocytes, T Lymphocytites, Lysozyme, Macrophages, Polypeptides, Properdin and Thiocyanate that are in the colostrum and milk as it comes from the ungulate and which may be extracted along with the desired unknown specific food factor.

Another satisfactory way of processing the colostrum and milk to extract therefrom the whey containing the specific food factor is to hold the same under refrigeration until the desired batch has been collected, and then passing the colostrum and milk, while at a temperature approximately that of the udder of an ungulate, through a filter that passes only food factors of the molecular weight of the class desired. Again, experience has shown a filter not greater than 0.2 microns to be satisfactory.

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In this manner, the food value of the factors is maintained while eliminating contaminants that may be in milk and colostrum.

In either process described above, the antigen'like material can comprise a solution of 10cc per teat of the ungulate with each cc having in solution a count of 750 million of the material. This has been found to be most effective when the antigen-like material is comprised of bacteria or virus, but when it comprises the blood of a sick animal, only 5cc of the blood is injected into each teat.

From the foregoing description, it will be apparent that either process of this invention produces a new and beneficial food product, including specific food factors having a molecular weight of less than 1200, and which food factors have been enhanced by the pre-partum introduction of a specific antigen-like material into the udder of the donor ungulate. In addition, the food product of this invention will contain all the factors present in the colostrum and milk of an ungulate that will pass through a 0.2 micron filter, such as B Lysin, Conglutinin, Interferon, Lactoferrin, Lactoperoxidase, B Lymphocytes, Lysozyme, Macrophages, Polypeptides, Properdin and Thiocyanate. The method of extracting the whey from the colostrum and milk as herein described also eliminates the contaminants normally present therein.

The invention is defined by the following claims:

We claim:

1. The method of producing a food product, comprising the steps of:

A. introducing pre-partum into the udder of an ungulate a specific antigen-like material selected from the group consisting of pollen, bacteria, virus, mold allergens, blood from sick animals, sperm and toxins;

B. removing secretory fluid from the udder of the ungulate thus treated;

C. removing the fat and solids from said secretory fluid so that only whey remain;

D. and passing said whey through a filter having a pore size of about 0.2 microns to effect separation from said whey of large molecules to produce a purified whey a portion of which consists of a food factor resulting from the introduction of said antigen-like material and having a molecular weight on the order of 1200 or less.

2. A product produced by the practice of claim 1.

3. The method of claim 1, wherein said secretory fluid comprises colostrum and milk.

4. A product produced by the method of claim 3.

5. The method of producing a food product comprising the steps of:

A. introducing pre-partum into the udder of an ungulate a specific antigen-like material selected from the group consisting of pollen, bacteria, virus, mold, allergens, blood from sick animals, sperm and toxins;

B. removing colostrum and milk from the udder of the ungulate thus treated;

C. separating the fat from the colostrum and milk;

D. thereafter freezing the colostrum and milk to effect precipitation of the milk curd solids therein;

E. gradually thawing said frozen colostrum and milk;

F. siphoning off clear whey from the thawed colostrum and milk;

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G. heating the remaining slurry portion of the colostrum and milk to a temperature of approximately 103 to 110 F;

H. mixing a dilute acid with said remaining slurry portion to produce a pH that causes coagulation of the milk curd solids therein;

I. separating said solids from the slurry so that only whey remains;

J. blending such remaining whey with the whey portion previously siphoned off;

K. and filtering said blend through a filter media having a pore size of about 0.2 microns to produce a whey permeate a fraction of which consists of a food substance resulting from the introduction of said antigen-like material and having a molecular weight of 1200 or less.

6. A product produced by the method of claim 5.

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Partial Reproduction of Patent 4,816,563

United States Patent **Patent Number: 4,816,563**

Wilson et al.

Date of Patent: Mar. 28, 1989

PROCESS FOR OBTAINING TRANSFER FACTOR FROM COLOSTRUM, TRANSFER FACTOR SO OBTAINED AND USE THEREOF

Inventors: Gregory B. Wilson; Gary V. Paddock, both of Mount Pleasant, S. C.

Assignee: Amtron, Inc., Charleston, S. C.

Appl. No.: 670,596

Filed: Nov. 15, 1984

Related U.S. Application Data

Continuation-in-part of Ser. No. 554,921, Nov. 25, 1983, abandoned.

Int. Cl[4] A61K 39/00; A61K 39/02; A61K 39/12; C07H 15/12

U.S. Cl. 530/344; 530/300;

Field of Search 424/95, 105, 88, 89, 424/92, 93; 514/2,7,8; 530/350,300,832, 833, 344, 300; 536/22, 23, 24, 27

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ABSTRACT

Antigen specific excreted transfer factor may be ob- tained by collecting material, e.g. colostrum or milk, secreted by the mammary gland of a suitable lactating mammal, e.g. a cow having immunity to the antigen under suitable conditions such that materials which interfere with transfer factor efficacy are removed so as to obtain transfer factor. Colostrum or milk collected may be used directly, typically after sterilization, or may be treated to further concentrate and/or purify transfer factor. Treatment to yield colostral whey containing transfer factor is presently the preferred method for obtaining transfer factor for use in conferring immunity against diseases associated with antigens for which the transfer factor is specific. Cell-asociated transfer factor specific for an antigen may also be obtained by incubation release from, or lysis of, cells obtained from the collected material. An alternative method for obtaining transfer factor is to recover it from the mammary tissue of a suitable lactating mammal. The transfer factor may be used in ediblecompositions and in methods for conferring immunity in a human or lower animal to a disease associated with the antigen. The transfer factor may then be used to prevent or treat the disease.

28 Claims, No Drawings

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PROCESS FOR OBTAINING TRANSFER FACTOR FROM COLOSTRUM, TRANSFER FACTOR SO OBTAINED AND USE THEREOF

BACKGROUND OF THE INVENTION

This application is a continuation-in-part of U.S. Ser. No. 554,921 now abandoned filed Nov. 25, 1983, the contents of which are hereby incorporated by reference into the present application.

During the first few days of lactation, the mammary gland secretes a fluid called colostrum which is quite different from normal milk. Both colostrum and milk contain antibodies of the humoral immune system and cells known to function in the cellular immune system including T cells, B cells and macrophages.(Watson, D. L., 1980, Aust. J. Biol. Sci. 33-403; Outteridge, P. M. and Lee, C. S., 1981, Adv. Exp. Med. & Biol. 137:513) The ratios and quantities of the various antibodies and cell types vary between milk and colostrum for a given species and between species (Watson, 1980; Outteridge and Lee, 1981). While antibodies produced in colostrum are known to be able to survive the infant digestive tract and confer immunity at least in some species (e.g. bovine), the various cell types found probably are less hardy and, if they do survive, are believed to provide immunity only to localized regions (Watson, 1980, Outteridge and Lee, 1981). Although Watson indicated that "the possibility remains that cell-mediated immune phenomena might be transferred from mother to young from the passage of soluble factors produced by lymphocytes such as transfer factor," neither Watson nor anyone else has reported either the transfer of cellular immuntiy using soluble products from colostrum or colostral cells, or the presence of transfer factor in colostrum or colostral cells. On the contrary, recent papers indicate that colostrum lacks optimal numbers of natural killer cells, Kohl, S., et al., 1978, J. Clin. Lab. Immunol. 1:221-224, Human Colostral Cytotoxicity, and that colostrum or milk block the ability of broad spectrum stimulants to induce cell mediated immunity, may block the killing of foreign cells by normal peripheral blood lymphocytes or neutrophils, and actually suppress cell mediated immunity when given to animals or mixed with cells in vitro Ogra, S. S. and Ogra, P. I., 1978, J. Pediatr. 92:550-555; Crago, S. S., et al., 1981, Clin. Exp. Immunol. 45:386-392. Moreover, since transfer factor was heretofore reported to be found only in or on lymphocytes, i.e. not in a cell-free state in large quantities, the presence of such transfer factor in elevated amounts in colostrum is totally unexpected and provided a readily available, inexpensive source for this otherwise rare and expensive material. Finally, the presence of T lymphocyte cells in colostrum does not meant that transfer factor will be present. It is well-known that serum and blood which contain lymphocytes do not contain transfer factor unless the lymphocytes are stimulated with antigen. Furthermore, all of the literature concerning transfer factor teaches that transfer factor should be a product of helper or inducer T cells. In order for colostrum to be of value as a source of transfer factor, helper T cells ought to markedly outnumber suppressor T cells (as in perepheral blood) since suppressor cells ar a source of products believed to negate effects or action of

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transfer factor. The relative ratios of helper or suppressor T lymphocytes have been reported to be lower in colostrum than in perepheral blood, leading to the conclusion that the physiologic role of T lymphocytes in colostrum is "not yet clear and cannot be predicted." Richie et al.,1982, *J. Immunol*. 129:1116-1119.

It is known that transfer factor can stimulate or transfer cell-mediated immunity against certain diseases in man and other animals and that this transfer can be made between species (Fudenberg, H.H., Wilson, G. B., Goust, J. M., Nekam, K., and Smith, C. L., 1980, in *Thymus, Thymic Hormones and T Lymphocytes,* Aiuti, F. and Wigzell, H., eds., London, Academic Press, p. 391; Wilson, G. B. and Fudenberg, H. H., Smith, C. L., 1980, Comp. Immunol. Microbial, Infec. Dis. 3:247). It is also known that transfer factor can be obtained from tissues such as blood serum leukocytes or lymph node lymphocytes but these sources require time consuming expensive leukophoresis or animal sacrifice and laborious extraction procedures (Wilsonand Fudenberg, 1983; Klesius, et al., 1980; Klesius, P. H. and Kristensen, F., 1977, Clin. Immunol. Immunopathol. 7:240; Wilson, G. B. and Fudenberg, H. H., 1981, Lymphokines 4:107). The yield of transfer factor is relatively small for the effort and quantity of tissue involved. It is further known that transfer inside immune cells from various tissues can be obtained via freeze-thaw lysis, and that it can be obtained by incubating these cells with or without antigens or organisms to release TF into the media (Wilson, G. B., Fundenberg, H. H., Paddock, G. V., Tsang, K. Y., Williams, A. M. and Floyd, E., 1983, in *Immunobiology of Transfer Factor,* Kirkpatrick, C. H. , Burger, D. R. and Lawrence, H. S. eds., New York, Academic Press, p. 331). It is also known that transfer factor is specific for a given antigen to which the source animal has received prior exposure or immunization (Wilson and Fudenberg, 1983; Wilson and Fudenberg, 1981) and that transfer factor of a

given antigen specificity can be obtained when leukocytes are incubated with that antigen or organism from which that antigen is derived (Wilson et al., 1983). Finally it is known that transfer factor for a given antigen can be induced by serial transfer of transfer factor for that antigen from an immune subject to another subject (Kirkpatrick, C. H. and Smith, T. K., 1976, Cell. Immunol. 27:323).

SUMMARY OF THE INVENTION

This invention provides an inexpensive process for obtaining transfer factor (TF) in virtually inlimited quantities from readily available sources. Specifically, excreted (TF) specific for an antigen may be obtained by collecting material secreted by the mammary gland of a suitable lactating animal, e.g. colostrum or milk from a cow having immunity to the antigen, under suitable conditions such that materials which interfere with TF efficacy are removed so as to thereby obtain TF. Preferably colostrum is employed as the TF source and is treated to separate cells, cells debris, caesin, immunoglobulins and other unwanted materials from colostral whey containing the TF.

If desired the transfer factor may be further concentrated or purified or both. Separation, concentration and purification methods which may be used include one or

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more of the following: centrifugation, extraction, precipitation, ultrafiltration, dialysis, chromatography and lyophilization. Alternatively, cell associated transfer factor may be obtained from the separated colostral cells by incubation release or by cell disruption. In addition to colostrum and milk, transfer factor may be obtained from the mammary tissue of a suitable lactating mammal.

The transfer factor so prepared may be incorporated into edible compositions or into pharmaceutical or veterinary compositions for the prevention or treatment of disease associated with an antigen for which it is specific, e.g. *Mycobacterium bovis, Coccidiodes immitis,* herpes simplex virus, bovine parainfluenza virus, Newcastle's disease virus, Marek's disease virus,infectious bronchitis virus, laryngotracheitis virus, a protozoan or a cancer-related antigen.

United States Patent **Patent Number: 4,843,065**
Collins et al. **Date of Patent: Jun. 27, 1989**

METHOD OF PRODUCING PRODUCTS FOR USE IN THE TREATMENT OF BACTERIAL AND/OR VIRUS INFECTIONS

Inventors: Robert A. Collins, 22 6th Ave.; Phillip F. Weighner, Rte.# 1, both of Waukon, Iowa 52172

Appl. No.: 108,937
Filed: Oct. 13, 1987

Related U.S. Application Data

Continuation-in-part of Ser. No. 736,268, May 22, 1985, abandoned, which is a continuation-in-part of Ser. No. 545, 000, Oct. 24, 1983, abandoned.

Int. Cl.[4] A61K 39/395
U.S. Cl. 514/21; 514/2; 514/8; 530/350; 530/414; 530/418; 530/832; 424/85.8
Field of Search.....424/85, 86, 87; 514/2, 514/8, 21; 530/414, 418,832

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***Primary Examiner*--Lester L. Lee**
***Assistant Examiner*--Jeff P. Kushan**
***Attorney, Agent, or Firm*--Ira Milton Jones**

ABSTRACT

A method of preparing remedies for the treatment of bacterial and viral infections which involves introduction into the udder of an ungulate during lactation, a specific vaccine comprising bacterial and/or viral organisms in an inactive state, and the preparation of small dosages of the secretary fluid subsequently withdrawn during lactation from the ungulate thus treated.

4 Claims, No Drawings

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METHOD OF PRODUCING PRODUCTS FOR USE IN THE TREATMENT OF BACTERIAL AND/OR VIRUS INFECTIONS

This application is a continuation-in-part of the application of Robert A. Collins et al. Ser. No. 736,268, filed May 22, 1985, itself a continuation-in-part of Ser. No. 545,000, filed Oct. 24, 1983, both now abandoned, and is also related to U.S. Pat. No. 3,376,198 and U.S. Pat. No. 4,402,938, issued Sept. 5, 1983.

The aforesaid copending application concerns the process of producing a homeopathic peoduct which involves the preparation of a homeopathic mother from selected raw material having either toxic of non-toxic characteristics and the conversion of said mother into a sarcode suitable for use as a homeopathic remedy.

U.S. Pat. No. 4,402,938 concerns a new and useful food factor for use as a nutritional supplement for animals involving introduction into the udder of an ungulate an antigen-like material which can comprise bacteria and/or virus in an active state.

U.S. Pat. No. 3,376,198 to Peterson et al. mentions Porter's suggestion of "manufacturing antibodies in the cow's udder by infusion of antigen into the udder of a lactating cow". The product produced by the method of applicants' invention which was shipped to Lobund for the Herpes tests, had the globulin (antibody carrying molecule) removed by ultra-filtration. The suggested product of Porter, the increase of antibody, is not the product of this invention. Applicants' invention is the production of a remedial product, consisting of the molecules remaining in whey after all globulin, as well as all other large molecules, are removed by filtration.

The product of this invention does not meet the definition of an antibody by any test, such as agglutination, electrophoresis, or gel diffusions. The product of this invention cannot be tested in vitro by any known biological tests available today, as opposed to the test for the product of Peterson et al. which is an in vitro antibody test.

The present invention, however, primarily concerns the production of a remedial product for use in the treatment of any bacterial and/or viral infection by a process involving introduction into the udder of an ungulate during lactation, a specific vaccine comprising killed organisms prepared from the infection to be treated, and the preparation of the dosages of from 1 to 5cc of the lacteal secretory fluid subsequently withdrawn from the ungulate thus treated.

The Peterson et al. patent is related to the present application in that it concerns the production of antibodies in milk by a process involving introduction of a specific antigen into the udder of an ungulate at spaced intervals during its pre-parturition period, that is, during pregnancy. The main objection to this procedure is that it requires an objectionabley long time, up to ninety days, before the ungulate give birth and the milk containing the desired concentration of antibodies only then becomes available.

In a more specific sense, this application concerns a method of producing a remedial product wChich can be used to treat viral infections such as Herpes or any other infection including bacterial infections such as leprosy.

In accordance with this invention, applicants introduce into the udder of an ungulate during lactation, a specific vaccine

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comprising inactive organisms prepared from the infection to be treated. During lactation, lacteal secretory fluid is removed from the ungulate a few days following such treatment and finally small dosages of said lacteal secretory fluid, from 1 to 5cc, are prepared, following the removal of larger molecules.

Viruses of the simplex Herpes virus (HSV-1) family are widespread and result in many diverse and severe diseases of man. Herpes virus, Varicella-Zoster virus and cytomegalovirus infect most individuals during childhood, Herpes virus type II (HSV-II) the causative agent of venereal disease, is less common, but is increasing in incidence at a tremendous and alarming rate, reaching epidemic proportions in the past several years.

After infection, which may be clinical or subclinical, these viruses may establish latent virus infections that may persist for life. HSV-I may result in fever blisters or cold sores, keratitis, or fatal encephalitis. Cytomegalovirus is the most important enviromental cause of congenital birth defects, Varicella-Zoster virus causes chickenpox as a primary infection with the recurrent form of the disease expressed as shingles.

In one method of most expeditiously practicing this invention for the production of a remedy for the treatment of Herpes or any other infection of the bacterial or viral type, a vaccine is first prepared from killed bacteria or virus of the disease to be treated. For this purpose a number of vials containing live bacteria or virus (for example eight) of 10 ml each, were heated at a temperature of 60^0 C., with occasional shaking, for four hours. The contents of the vials were then pooled,and small aliquots were removed for plaque assay in Vero cells to test for hear inactivation. The Herpes passage 4 virus titer was 1.5×10^6 plaque forming units per ml. No infectious Herpes was dectectable by plaque assay after such treatment at 60^0 C., for four hours.

The Herpes vaccine was infused at four different times into the udder of a selected ungulate at approximately ten-day intervals, at a rate of 5cc per quarter per infusion. The vaccine thus produced was then stored in a frozen state (0^0 F.) for preservation until used.

In one test, the withdrawal of lacteal fluid from the ungulate thus treated was started three days following the infusion period and was repeated for a period of approximately two weeks. The collected fluid was then pooled and (using methods known to the art, such as centrifugation and precipitation) the fat and casein were removed to produce a whey product. However, for oral administration, it is not necessary to remove the fat or the casein.

Two (five gallon) refrigerated tanks marked 1 and 11 were set up in the lab and piped to a custom-built lab model ultra filter, equipped with a 0.2 micron membrane and a 3-horsepower direct drive pump capable of maintaining 60 psi pressure on the high side of the ultra filter while processing. The inlet on the pump was piped to the outlet of Tank 1. The piping was arranged so that the concentrate from the filter would be returned to the top of Tank 1 and the filtrate would be collected in Tank 11.

A preservative was prepared as follows:

11.25 gm methyl paraben

3.75 gm propyl paraben

2.46 gm NaOH pellets

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and was placed in a 500 ml erlenmeyer flask. Hot distilled water was added while swirling until all were dissolved. Approximately 100 ml distilled water was used.

Ten liters of the whey product processed above was put into the refrigerated Tank 1. The 100 ml preservative produced as described above, was added to the whey product in Tank 1 while stirring to obtain a homogeneous solution.

The ultra filter was started and run for two hours. The refrigerated tanks kept the temperature below 100^0 F. The filtrate collected in Tank 11 was then filtered using a Seitz filter equipped with a 0.02 micron filter. From this point on, all work was done in a sterile room equipped with a high efficiency air filter system. This product was then sterile-filtered by passing through an inline sterile filter equipped with a sterilizing filter cartridge.

The final sterile product was then bottled in sterile 20 ml ampules, that were sealed using a double flame ampule sealer. Ten percent (10%) of the vials were then tested for sterility.

Small dosages, for example 1 to 5cc of the resulting product can be used in either the liquid form, diluted or undiluted, or in a dried state when encapsulated. Drying can be readily accomplished by freezing.

A product made earlier in the same way, except that infusion of the vaccine was performed pre-partum, was tested on mice at the Lobune Institute of the University of Notre Dame. Those tests revealed that there was a statistically significant decrease in the death rate of mice protected by the lacteal secretion of Herpes infused cows when challenged with a lethal dose of Herpes virus. Tests made thus far on the product produced by infusion during lactation indicate that the same efficacy of the product can be acheived in as little as three days following the infusion period.

Further testing of this latter product is currently being done at the laboratories of D & S Associates in Madison, Wis.

The term "small dosages" as used herein and in the claims can be defined as quantities as small as 1.0 ml to 0.5 ml, or up to 1 to 5 cc. Of significance is the fact disclosed by this earlier testing that, in some instances, the smaller (0.5 ml) dosages were more effective than the larger dosages. However, doses even smaller than 0.5 ml also have been found to be effective. In the earlier test cases it was found that "a large statistically significant increase in resistance to HSV-1" was achieved in mice challenged with that virus after injection of 1.0 ml per day of the product produced by the instant method, over a period of eight days.

A product suitable for use in the treatment of bacterial infections can be produced in the same way as described

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herein, except that the vaccine introduced during lactation into the udder of the selected ungulate is prepared from the bacterial infection to be treated. Again, in this case, the active organisms in the bacteria are killed to render the vaccine completely inactive.

From the foregoing description, it will be apparant to those skilled in the art that the remedial product of this invention provides an effective treatment for viral and bacterial infections for which there was heretofore no known remedy.

The invention is defined by the following claims:

We claim:

1. The method of producing a remedial product useful in the treatment of bacterial and/or viral infections consisting essentially of:

A. preparing a vaccine of killed microrganisms of the infection to be treated;

B. during lactation, introducing into the udder of an ungulate by infusion or injection, the vaccine comprising killed microrganisms prepared from those of the infection to be treated;

C. removing lacteal secretory fluid in about two days from the ungulate thus treated;

D. filtering out larger molecules including antibodies from lacteal secretory fluid with approximately a 0.2 mi cro filter; and

E. preparing dosages of the remaining lacteal secretory fluid proportional in amount to the size of the animal to be treated.

2. The method of claim **1** further comprising the removal of fat from said lacteal secretory fluid prior to preparation of said dosages.

3. The method of claim **2** further comprising the removal of casein from siad lacteal secretory fluid prior to preparation of said dosages.

4. The method of producing a remedial product useful in the treatment of bacterial and/or viral infections consisting essentially of:

A. during lactation, introducing into the udder of an ungulate a vaccine comprising killed microorganisms prepared from those of the infection to be treated;

B. removing lacteal secretory fluid from the ungulate thus treated in about two days after introduction into the udder;

C. filtering out larger molecules including antibodies from the lacteal secretory fluid with approximately a 2 micron filter and pressurizing fluid on the inlet side;

D. preparing approximately 1 to 5cc dosages of the filtered fluid.

****

United States **Patent Number: 5,102,669**
Collins
Date of Patent: Apr. 7, 1992

METHOD OF PRODUCING REMEDIES AND PRODUCTS OF THE METHOD

Inventor: Robert A. Collins, 22 6th Ave. NE., Waukon, Iowa 52172
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Continuation-in-part of Ser. No. 86,539, Aug. 18, 1987, abandoned, which is a continuation-in-part of Ser. No. 609,277, May 11, 1984, abandoned, which is a continuation-in-part of Ser. No. 528,881, Sept. 2, 1983, abandoned.
Int. Cl.[5] A61K 35/20
U.S. Cl. 424/535; 424/85,8; 424/86; 424/87;
Field of Search 424/85, 87, 95, 105, 424/535; 85,8,86

References Cited

U.S. PATENT DOCUMENTS

3,376,198 4/1968 Peterson et al. 424/85
3,553,317 1/1971 Michaelson et al. 424/87

OTHER PUBLICATIONS

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ABSTRACT

A method of converting allergenic substances which may have medicinal value into a new, safe and effective non-toxic and novel product having utility as a homeopathic remedy. This invention contemplates converting toxic substances into useful medicaments by a process involving the mammary glands of animals.

12 Claims, 1 Drawing Sheet

Drawing

Figure 1
Old

Obtain Raw Product
Any Product Having
Medicinal Properties

–

Put Raw Product in
Alcohol Solution to
Produce a Homeopathic Mother

–

–

Establish the
Desired Potency by
Decimal Serial
Dilution

Figure 2
New

Obtain Raw Product
Any Product Having
Medicinal Properties

–

Put Raw Product In
Solution with a Non-Irritating Vehicle
to Produce a Homeopathic Mother

–

Introduce the Homeopathic Mother Into the Udder of a Mammal Prior to Parturition

–

Collect the Lacteal Secretion After Parturition

–

Establish the
Desired Potency by
Decimal Serial
Dilution

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METHOD OF PRODUCING REMEDIES AND PRODUCTS OF THE METHOD

Webster's 3rd International Dictionary defines homeopathy at page 1033, as follows: "a system of medical practice that treats a disease by the administration of minute doses of remedy that would in healthy persons produce symptoms of the disease treated."

In the known art of producing homeopathic remedied and in accordance with the principles, methods and terminology described in the Homeopathic Pharmacopoeis of the United States, Eighth Edition 1979; Supplement A-1982 and Compendium of Homeotherapeutics 1974, a raw product is placed either in solution of mixed with lactose to provide a starting solution or mixture known and hereinafter referred to as a mother. The starting solution or mixture is thereafter attenuated in the case of liquids or triturated in the case of insoluble substances to produce a product having homeopathic characteristics which are the same as those of the raw product used in the production of the mother. It should be noted that attenuation or trituration are the terms now used to describe the process of potentizing a substance by dilution and succession.

While this known method can produce a homeopathic remedy that is useful in many instances, there is a definite danger associated with the prior art method when a raw material used in the production of the mother is either a nosode originating from a microorganism, a material resulting from the disease process, a toxin of natural origin, or a toxic chemical or metal. This is especially true in the event of use when the remedy is not needed, since the continued use of the homeopathic past that point of time when the symptoms of the condition being treated have disappeared, can cause those same symptoms to reappear.

Petersen et al. U.S. Pat. No. 3,376,198, Method of Producing Antibodies in Milk, is a related patent. The Petersen et al. patent shows use of anti-genetic raw material for use in a non-pathogenic condition. As an example, it specified that the "antigen was dead

salmonella pullorum." The Petersen et al. patent does not use the first mother of a toxic or pathogenic raw material for infusion into the udder of an ungulate and therein converting the first mother into a second mother having the same homeopathic characteristics as the raw material used in the first mother without any of the toxic or pathogenic characteristics that were present in the raw material used in the production of the first mother.

The Petersen et al. patent uses the production of antibodies primary for use in the prevention of disease. Hence, Petersen et al. could be said to produce a product which is similar to and acts like a vaccine for protection against disease. In this respect, it should be noted that throughout their specification Petersen et al. refer to the "protection principle of their invention," Petersen et al. thus has as aprimary concern, the production of a specific antibody to antigens for the stimulation in the treated animal of such antibodies or "protective agent" for a new approach to the prevention of disease in animals.

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Petersen et al. does not teach the use of any antigens such as those either toxic or pathogenic properties whereas the applicant's invention involves the production of a first mother from any selected raw material, even those having toxic or pathogenic characteristics.

Michaelson et al. U.S. Pat. No. 3,553,317, IGA Antibody from Lacteal Fluids, is also similar, but is not concerned with the production of homeopathic products by means of a process such as set forth in the claims of the application. Michaelson et al has an objective, the production of a product which he identifies as lactimunin having a molecular weight of 40,000-100,000. He explains that lactimunin is a new antibody. The product produced by the applicant is produced by a different
process and is not an antibody, and moreover its molecular weight is less than 2000.

The Michaelson et al patent does not show the production of a first mother using raw material having either a toxic or a non-toxic or a pathogenic property, nor infusion of the first mother into the udder of an ungulate to therein produce a second mother having the same homeopathic properties that had been present in the first mother.

Accordingly, it is not believed that the Michaelson et al patent anticipates the applicant's invention.

By definition, the applicant's final produce is a minute fraction of the original crude substance used to produce the first mother. This product has been in effect filtered through the udder of an ungulate in this process of producing a homeopathic-like product. This process and product are not the same as shown in either Petersen et al or Michaelson.

The Petersen and Michaelson patents show processes for producing antibodies. An antibody is a protein substance in the blood or tissue of animals that destroys or weakens a specific bacteria in vitro.

The product of the instant invention does not destroy bacteria. The product of the instant invention will not agglutinate specific bacteria in vitro. The action of a product of the instant invention is that it signals the body to expel the specific bacteria which is the crude product used to produce the first mother. It may also interfere with the colonization of a specific bacteria.

Accordingly, it is not the same process or product as set forth in the Petersen or Michaelson patents. Accordingly, these patents are not believed to anticipate the applicant's invention.

In contrast, it is an object of this invention to provide a method of producing a medicinal product having homeopathic characteristics, which method involves the production of a first mother either toxic or non-toxic properties, and which method is characterized by utilization of said mother to produce a new or second mother which has the same homeopathic characteristics minus any toxic properties present in the first mother.

More specifically, it is a purpose of the invention to produce a homeopathic remedy which involves production of a first mother into the mammary gland of a mammal for conversion therein to a second mother having the same homeopathic characteristics as the raw material used in the production of the first mother, but without any harmful toxic properties that may have been present in the raw material used in the productionof the first mother.

It is a further object of this invention to produce an entirely safe homeopathic remedy from raw products that include, but are not limited to, the following: Chemical products of natural or synthetic origin, animal sub-

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stances, allergens such as molds, pollens, house dust, fungus, hair and dander, toxins, parasites and microorganisms such as bacteria and virus, sperm.

It is still another object of this invention to infuse a homeopathic substance into the udder of a mammal, to therein effectively remove the substance itself while transferring its homeopathic characteriatics to the lacteal secretion.

With these observations and objectives in mind, the manner in which the invention achieves its prupose will be appreciated from the following description and the accompanying drawing, which exemplifies the invention, it being understood that changes may be made in the precise method of practicing the invention without departing from the essentials of the invention set forth in the appended claims.

The accompanying drawing diagrammatically illustrates a comparison between the old and new methods of producing the homeopathic remedy of this invention, in which:

FIG. 1 is a block diagram illustrating the known method of producing products having homeopathic characteristics; and

FIG. 2 is a similar block diagram illustrating the method of this invention.

The main distinctions are of substantial importance and reside in:

(1) the raw material for production of the desired homeopathic remedy can be one which is either toxic or non-toxic in nature; and

(2) the vehicle use in producing the homeopathic mother should be a non-irritant, as distinguished from the conventional vehicle, preferably whey, distilled water or a physiological saline solution.

In a more specific sense, the first step of obtaining the raw material in the practice of the invention may be substantially the same as the first step in producing a homeopathic remedy as outlined in the Homeopathic Pharmacopoeia of the United States, Eighth Edition 1979 and Supplement A-1982. The raw material may be any chemical product of natural or synthetic origin, biological preparations in the wider sense, and any substance which may be considered to have medicinal value such as--but bot limited to--all the substances listed in the Homeopathic Pharmacopoeia of the United States, Eighth Edition 1979.

However, the raw product or medicinal substance chosen to produce the homeopathic remedy in accordance with this invention can be either of a toxic or non-toxic nature, and it si then put into suspension according to the procedure laid out in the Homeopathic Pharmacopoeia of the United States, Eighth Edition 1979 and Supplement A-1982, with the exception of the solvent. The ethyl alcohol prescribed in the Homeopathic Pharmacopoeia of the United States Eighth Edition 1979 is such an irritant and according to this invention is replaced with a non-irritating vehicle. I have found physiological saline, distilled water and/or a purified whey in which the solids are over 80% (eighty percent) lactose to be good non-irritating substitutes for alcohol. Such materials are available on the market.

The purified high lactose whey can be produced using a high speed continuous centrifuge that will remove all particles over a 0.4 micron size. This high lactose whey is preferably then sterilized by passing it through a 0.2 micron sterilizing filter.

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Any mammal may be used in the practice of this invention. Cows and goats were used, but cows were found to be the most practical.

Any method can be used to introduce the homeopathic mother (the first mother) into the cistern of the udder. This can be done either before or after parturition. Two methods have been used in the practice of this invention: infusing the first mother into the cistern through the orifice of the teat canal, using a sterile 10cc syringe equipped with a blunt cannula; or, alternatively, injecting the side of the udder using a 10cc sterile syringe equipped with a needle of suitable length. The infusion method has been found to be more feasible for repeated doses but requires more care to maintain sterility of the equipment.

A satisfactory dose of the first mother inserted into the udder of each cow, or other mammal, has been found to comprise 10cc per quarter of a sterile suspension of a specific antigenic extract having about 3260 P. N. U. (Protein Nitrogen Units) per cc. Allergenic extracts are a commercially available product and comprise the allergens mentioned hereinbefore.

Regardless of which allergens are used in the production of the first mother, a 10cc dose of the solution of the first mother, prepared as outlined above, is preferably infused into each quarter of a cow, using aseptic techniques, tow or three times at 7 to 12 day intervals prior to parturition. Lactating cows may be used but the use of dry cows has been found to be less upsetting to the cow.

When dry cows are infused, the colostrum and first milk as it comes from the cow after parturition is saved and is used as a second mother for the preparation of a homeopathic product by accepted methods of attenuation.

This invention will produce a homeopathic product that is effective in overcoming disease that in many instances a regular homeopathic product, made from the same starting material, was found to be ineffective.

In the practice of producing homeopathic remedies, a life-death challenge test is not used. With the method of the instant invention of utilizing the cow to produce a second mother for the production of a homeopathic product, a life-death challenge test is feasible.

The following experiment was carried out to establish the potency of a product produced by the method of this invention. Experimental procedure and results of challenge follow.

A smooth colony of a pathogenic *pseudomonas aerogenosa* cultured from a veterinary posting specimens taken from diseased claves, was asceptically transferred to media and processed into a vaccine by methods known in the art. The vaccine was heat-killed, corrected to a density of McFarland 5, and bottled in 40ml sterile serum bottles, capped with a sterile rubber stopper. A second calf Holstein heifer was health-checked by a veterinarian. This cow was infused with 5ml of the above vaccine, intermammary, three times at weekly intervals just prior to parturition.

When the cow calved, one gallon of colostrum was saved in a gallon jug market "A" and refrigerated, and one gallon of milk was saved in a gallon jug marked "C" and refrigerated. One ml colostrum from jug "A" was vigorously mixed with 9ml sterile distilled water in a 20ml test tube and capped with a sterile rubber stopper. This process was carried out in a sterile room under a Hepa filter. 1ml of this dilution was

mixed with 9 ml sterile distilled water and vigorously mixed by shaking and vortexing the fluid.

1ml of this 2nd serial dilution was diluted with 9ml sterile distilled water and vigouously mixed as above, in a 20ml test tube. This 3rd serial dilution was then bottled in sterile 20ml serum bottles, capped with a sterile rubber stopper and sealed with an aluminum crimped seal. This was marked A-3x 1ml colostrum from the jug marked "A" was serial diluted in the same manner described above for six serial dilutions. The sixth dilution was sterile bottled in 20ml serum bottles using the technique described above. This bottle was marked A-6x.

1ml milk from the jug marked "C" was serial diluted with 9ml water, vigorously mixed and vortexed in a 20ml test tube. This process was carried out to 3 serial dilution in the same manner as above. The product of the 3rd dilution was then sterile bottled in 20ml serum bottles, capped with a sterile rubber stopper and sealed with an aluminum crimped seal. This bottle was marked C-3x.

1ml milk from the jug marked "C" was diluted with 9ml sterile distilled water in a 20ml test tube, stoppered and vigorously mixed by shaking and vortexing. This process was carried out for a total of six serial dilutions. The product of the sixth serial dilution was then bottled, capped and sealed as above. This bottle was marked C-6x.

The four products marked A-3x, A-6x, C-3x, and C-6x were then tested on mice previously injected I. P. with a lethal challenge of pathogenic *pseudomonas aurogenosa* at the rate of 25 X 10^6 per ml. Results were as follows:

Type of raw product used to produce 2nd mother	**Treatment** Dosage 1ml	**Pseudomonas** Challenge	**Results** Alive	Siick	Dead
		TEST 1			
NON USED**	WATER	25 x 10^6	1	0	3
NONUSED	2mg eq. 390^0	"	4	0	0
COLOSTRUM	A 3x	"	2	0	2
COLOSTRUM	A 6x	"	3	0	1
MILK	C 3x	"	1	0	3
MILK	C 6x	"	3	0	1
NON USED**	Water (one mouse)	0	0	1	0
	Dosage Varied	TEST 2			
NONUSED**	WATER	25 x 10^6	1	0	3
NON USED	2 mg. eq. 390^0	"	4	0	0
COLOSTRUM	1 cc A 3x	"	3	0	1
COLOSTRUM	.5 cc A 3x	"	4	0	0
COLOSTRUM	.25 cc A 3x	"	4	0	0
MILK	1 cc C 3x	"	3	0	1
MILK	.5 cc C 3x	"	4	0	0
MILK	.25 cc C 3x	"	3	0	0
NON USED**	Water	0	4	0	0

4 mice per group

390^0 = our positive control

A = Colostrum used as a raw material to produce the second mother

C = Miilk used as raw material to produce the second mother

** = Control

Tests conducted at Derse Schroeder Laboratories, Madison, Wisconsin

The first mother may be either a Class A or a Class L raw medicinal product. These products are defined in the Homeopathic Pharmacopoeia of the United States, pages 54 and 65 respectively, of the Eighth Edition, first Supplement. As therein seen, Class L products are pathogenic or toxic.

The second mother produced in accordance with the method described above, is always a Class A material. This is true even when the first mother used in the production is a Class L or pathogenic substance.

From the description thus far, it will be noted that the practice of my invention is a two-phase operation. The first phase involved the production of a homeopathic mother to be used in the production of a second mother.

An example of the method I have employed in producing the first mother consisted in the use of 100cc of specific *pseudomonas aurogenosa*

vaccine prepared by methods well known in the art, inactivated by heat and corrected to a concentration of McFarland 5 density. McFarland 5 density is a term used to designate the potency of a vaccine and is commonly used by persons skilled in the art of preparing vaccines. McFarland density is a scale of densities and McFarland 5 is a density of 1500 x 10^6 bacterial ml.

Using sterile techniques, 60cc of the above pseudomonas aurogenosa vaccine was diluted with 60cc of sterile whey.

The first mother was sterile bottled in these 40cc vials equipped with sterile rubber sleeve stoppers and stored under refrigeration for later use in the production of a second mother. The 40 40cc vial size was employed for convenience in later infusion into the udder of the cow, 10cc per quarter.

Another example of producing a first mother for use in the second phase of my invention involves the use of an insoluble metal as the raw medicinal product. Aluminum is such an insoluble material. In this case I added one gram of water-soluble aluminum orotate to 99cc of distilled water to produce a solution. At this point 20cc of the above solution was added to 20cc of purified whey that had been previously filtered through a 0.2 micron filter to produce one animal infusion in the case of a cow, or two animal infusions for goats.

This first mother was stored under refrigeration for use in the production of the second mother in the second phase of the invention.

The second phase of this invention involves the production of a second mother possessing the homeopathic characteristics of the first mother. This process may begin with a lactating animal or during its dry period.

An example of the method of producing the second mother

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second or later calf, about one month prepartum. The udder and teats are prepared and treated in the following manner.

(1) Wash with water and soap and rinse with clean water;

(2) Dry with individual paper towels:

(3) Cover test opening (or point of injection if one chooses to go through the side of the udder) with a cotton swab previously soaked in a 70% alcohol solution;

(4) Fill four 10cc syringes with the previously prepared first mother. using a sterile syringe needle for withdrawal from the bottle;

(5) When introducing the substance into the udder via the teat canal, remove the needle from the syringe and replace with a sterile cannula;

(6) Remove the alcohol swab and inset the blunt cannula into the orifice of the teat and expel the contents into the cistern of the quarter. All must be done in an aseptic manner. If the cannula is accidentally contaminated by touching the side of the teat or the operator's fingers, it should be discarded and replaced with a sterile cannula.

A separate syringe and sterile cannula should be used for each quarter. This procedure should be repeated two or three times at seven to ten day intervals prior to parturition. At parturition, for the production of a high potency product of this invention, a few pounds of the colostrum and milk is saved in well-marked containers and frozen for storage. Prior to freezing the colostrum and milk is filtered through a 0.2 micron filter which filters out large molecules and antibodies. An 0.1 micron filter may be used which will filter out smaller molecules and antibodies. It is not necessary that the milk be filtered as long as some suitable means of separating out the larger molecules is used.

1cc of this colostrum can now be used to produce a second mother by adding 1cc of the colostrum or milk to 9cc of water, or water and ethyl alcohol, to produce a 10% (10:1) liquid attenuation which is designated IX. The best method to get this in solution is with the use of a Vortex mixer.

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This serial dilution and succession is repeated, using 1cc of the previous mixture and 9cc of distilled water or alcohol until the desired solution is arrived at.

For purposes of the study hereinafter referred to, two products were prepared in accordance with the previously outlined steps of the method of this invention, namely:

(1) prepare the first mother using *pseudomonas aerogenosa* vaccine;

(2) infuse the cow with such first mother to product the second mother;

(3) prepare two test products of potency of 3X (1:1000 dilution) and 6X (1:1, 000,000 dilution).

In order to establish the utility of a product produced by the method of my invention described above, a series of challenge and protection tests were conducted using mice to establish the efficacy of this homeopathic product.

First, in the establishment of a lethal dose, it was found that 25 X 10^6 organisms of a specific pseudomonas injected I.P. would kill two out of three mice. All mice indicated were challenged with 25 X 10^6 specific pseudomonas organisms I.P.

The first test was performed to observe the effect of a 1cc injected I.P. of a 3x and 6x homeopathic remedy prepared using one gram of colostrum or one gram of milk, to produce the second mother and then serially diluting and succusing 1cc of the second mother and 9cc of distilled water to a dilution indicated as either 3x or 6x.

The second test was conducted to indicate the effect of varying the dosage of the homeopathic remedy.

These tests, depicted on the following chart, prove the efficacy of the homeopathic remedy of this invention.

Type of raw product used to produce 2nd mother	TREATMENT	PSEUDOMONAS CHALLENGE	RESULTS Alive	Sick	Dead
	Test 1				
	WATER	25 x 10^6	1	0	3
	2mg. eq. 390	"	4	0	0
COLOSTRUM	A 3x	"	2	0	2
COLOSTRUM	A 6x	"	3	0	1
MILK	C 3x	"	1	0	3
MILK	C 6x	"	3	0	1
	Water (one mouse)	0	1	0	0
	Test 2				
	WATER	25 x 10^6	1	0	3
	2mg. eq. 390	"	4	0	0
COLOSTRUM	1cc A 3x	"	3	0	1
COLOSTRUM	.5cc A 3x	"	4	0	0
COLOSTRUM	.25cc A 3x	"	4	0	0
MILK	1cc C 3x	"	3	0	1
MILK	.5cc C 3x	"	4	0	0
MILK	.25cc C 3x	"	3	0	1
	WATER	0	4	0	0

4 mice per group
390 is our positive control for protection of animal
A colostrum used to produce the second mother
C milk used to produce the second mother
Tests conducted at Derse-Schroeder Laboratories, Madison, Wisconsin

It is important to note that in accordance with this invention, the introduction of the first mother into the udder of a mammal effects a conversion therein of the raw material into a new and different cells which, however, have the same homeopathic characteristics as the raw material used in the production of the first mother.

EXAMPLE 1

One hundred and thirty (130) milk samples were collected from cows (in four herds) that had visible udder congestion and/or abnormal milk. These samples were streaked on EMB and blood agar with azide plates. These prepared plates were then incubated at 37^0 C. for twenty-four (24) hours, after which screening for pathogens was carried out. From these specimens, a colony of staphylococcus aureus was transferred, via aseptic technique, to media and processed into a vaccine by methods known in the art, thus producing the first mother. This vaccine was then heat-killed and standardised to a density of McFarland 5, a standard used in the preparation of vaccines. The vaccine was then bottled aseptically in 60cc serum-type glass vials, capped with sterile rubber stoppers and sealed with aluminum seals. It was marked Staph-1 for identification. A code number was also assigned.

For the production of a second mother, a cow 3-4 weeks prepartum was selected. A visible health check was made by a veterinarian, along with a brucella and TB test. Care was taken to see that the teats were clean and dry prior to infusing. Each teat was dried after washing with an individual paper towel. Each teat was then covered with a thin cotton pad soaked in 70% alcohol and left a few minutes.

Four sterile 5cc syringe equipped with an 18 guage hypodermic needle was filled with the vaccine from the bottle marked Stap-1, previously prepared. The hypodermic needles were then disconnected from each syringe and replaced with a sterile plastic canulae. As each canulae was attached, the anulae end of the syringe was stored in an open sterilizing bag for protection. The cow was then infused, through the teat opening, using prepared syringes.

The infusion was repeated at seven-day intervals for a total of three infusions. Detailed records were maintained, including the cow's identification, the vaccine dose, dates and times of infusion, date of calving and the initials of the person doing the work.

Preferably when the cow is calved, the cow was milked and the milk was filtered with a 0.1 micron filter to filter out antibodies. One gallon of this filtered colostrum and early milk was saved in a gallon plastic jug.The jug was tagged, using a waterproof tape, showing the date, vaccine code and the cow number or name. The identification, Staph-1, was also put on the jug, using permanent magic marker. The jug with the Staph-1 colostrum was frozen for storage.

Three additional pathogens were selected from the above screen, specifically:

1. a *a streptococcus agalactae* colony
2. a *g streptococcus agalactae* colony
3. An *E. Coli* colony

The same procedure that was used to produce the Staph-1 product, detailed above, was employed to produce a product starting with each of the isolates listed above. Three 2nd-calf Holstein cows, all about one month prepartum, were selected. One for each of the three additional products to be produced. One for the *a streptococcus agalactae,* one for the *g streptococcus agalactae* and one for the *E. Coli*.

As these cows calved, one gallon of colostrum was saved in a plastic jug. The jug was tagged with the code assigned the isolate referenced and the cow number or name. The jug was then frozen for storage. When all

three jugs were frozen, they were thawed, along with the jug coded Staph-1 produced earlier.

One ounce was removed from each of the four jugs and put in an 8 oz wide-mouth screw top jar and capped with a metal cap. These four products were thoroughly mixed by shaking and rolling end over end. The jar was coded with each of the four codes used to identify each isolate and each cow used to produce the four individual components of this jar.

From this point-on, all work was carried out under a Hepa filter, using aseptic procedures, by gowned and masked technicians, wearing sterile rubber gloves.

One ml of the product in the jar with the four components was withdrawn using a sterile pipette. This was added to 9ml sterile distilled water in a 20ml sterile test tube, stoppered with a sterile rubber stopper. This tenfold dilution was vigorously mixed by shaking and vortexing.

One ml of this first serial dilution was then diluted with 9ml sterile distilled water and thoroughly blended as above. This process was carried out for six serial dilutions.

The product of the sixth serial dilution was bottled in 50ml sterile serum type bottles, capped with a sterile rubber cap and sealed with an alumin seal. Ten 50cc bottles were then sent to the veterinarian doing the research.

Each month the cows in a herd having high cell counts are listed on the owners DHIA report for treatment. The high cell count cows in the herd were treated with 2-4cc (ml) doses of the product orally on their feed at twelve-hour intervals, with the following results:

Problem cows in herd code DM-10
High Somatic Cell Count (SCC), March 1987

Cow No.	SCC on March 5	TREATMENT	SCC on March 20
66	>1,000,000	2-4cc MT on feed	<200,000
65	"	"	<200,000
60	"	"	>1,000,000
82	"	"	>1,000,000
172	"	"	1,000,000
146	"	"	<200,000
69	"	"	<200,000
173	"	"	<200,000
200	"	"	<200,000
136	"	"	<200,000
124	"	"	<200,000
150	"	"	<200,000

June 1987

Cow No.	SCC on June 17	TREATMENT	SCC on June 22
82	>1,000,000	5cc MT, 2-4 times 12 hr Interval on feed	<200,000
52	"	5cc MT, 2-4 times 12 hr Interval on feed	<200,000
154	"	5cc MT, 2-4 times 12 hr Interval on feed	<200,000
151	"	5cc MT, 2-4 times 12 hr Interval on feed	<200,000
37	"	5cc MT, 2-4 times 12 hr Interval on feed	<600,000
196	"	5cc MT, 2-4 times 12 hr Interval on feed	>1,000,000
120	"	5cc MT, 2-4 times 12 hr Interval on feed	<200,000
140	"	5cc MT, 2-4 times 12 hr Interval on feed	<200,000
464	"	5cc MT, 2-4 times 12 hr Interval on feed	<200,000
60	"	5cc MT, 2-4 times 12 hr Interval on feed	>1,000,000

continued

61	"	5cc MT, 2-4 times 12 hr Interval on feed	<200,000
75	"	5cc MT, 2-4 times 12 hr Interval on feed	<200,000

Note: Only one cow, #60, repeated in the second list in June. The necessity of reducing a high cell count in a dairy herd is essential in selling milk. Herds with cell counts over one and one-half million are prohibited from selling their milk on the market.

EXAMPLE 2

Three of the four jugs of colostrum produced for Example 1 above were removed from the freezer and thawed. 25ml was transferred from the jug with the Code Staph-1 and put in a 6oz glass jar. 25ml was transferred from the jug marked *a* strep and transfreed to the same 6oz jar. 25ml of the product in the jug marked *y* strep was transferred to the same 6oz glass jar. A 25ml pipette was used to make the above transfers.

The 6oz jar was capped and thoroughly blended by shaking. 1ml of the product in this 6oz glass jar was transferred to a 20ml sterile test tube containing 9ml sterile distilled water. This transfer was accomplished by use of a sterile pipette. This test tube was stoppered with a sterile rubber stopper and vigorously mixed by shaking and vortexing.

1ml of this first 10-fold dilution was aseptically transferred to a second 20ml sterile test tube containing 9ml sterile distilled water. This serial dilution was mixed by vigorously shaking and vortexing. This process was carried to the 6th serial dilution.

On the 5th and 6th d, ilution, all of the product was processed.

The 6th dilution was sterile bottled in 60cc serum bottles. The label, serial number and code were referenced to the original culture.

Ten 50ml bottles of this coded product were delivered to the veterinarian. Eighteen (18) cows in five herds, with clinical mastitus were treated with this 6th dilution product. Following are the results:

RESULTS

Cow Identification	Condition	Treatment Amount	Number of Treatments	Hours to Return to Normal
#11RN	Clinical	10cc IU*	2	36
#33RN	Clinical	10cc IU	2	36
#7RN	Clinical	10cc IU	3	48
#20JS	Clinical	10cc IU	3	48
#38JS	Clinical	10cc IU	2	36
#39JS	Clinical	10cc IU	1	24
#53JS	Clinical	10cc IU	2	60
#57JS	Clinical	10cc IU	1	48
#79TH	Clinical	10cc IU	4	48
#14TH	Clinical	10cc IU	3	48
#23JS	Clinical	10cc IU	2	24
#84JS	Clinical	10cc IU	1	24
REDJS	Clinical	10cc IU	2	36
WHITEJS	Clinical	10cc IU	2	24
#180CT	Clinical	10cc IU	3	Failed
#H21CT	Clinical	10cc IU	4 + 3 orally	Failed
#R23CT	Clinical	10cc IU	2	Partial
#46JA	Clinical	10cc IU	4	Failed

There is a great economic advantage in getting clinical cows back to normal without the use of antibiotics. This is due to the milk throwaway required when antibiotics were given a lactating dairy cow.
*Inter udder

From the foregoing description together with the accompanying drawing, it will be apparent to those skilled in the art that

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this invention provides a new and improved process for producing a homeopathic product superior to any heretofore produced.

The invention is defined by the following claims:

1 claim:

1. In the process of producing a homeopathic product having a molecular weight of less than 2000, the steps of:

A. selecting an allergenic raw material having either toxic or non-toxic or pathogenic or non-pathogenic characteristics;

B. combining such material with a vehicle which is non-irritating to tissue to produce a combination hereinafter referred to as a homeopathic first mother;

C. introducing a homeopathic mother into a mammal's udder effecting conversion of the raw product in said combination into a secretion hereinafter referred to as a second mother having the characteristics of a sarcode and the homeopathic characteristics of the first mother, and not depending on antibodies as a remedy;

D. removing the second mother from the udder and separating out and disposing of larger molecules including antibodies from the second mother which are approximately 0.2 micron and larger; and

E. serially diluting said second mother to 10^3 to 10^{30}.

2. The process of claim 1, wherein said conversion is effected in the udder of an ungulate.

3. The process of claim 1, wherein said combination is introduced into the udder of a cow or goat, to therein effect said conversion of the raw product into a sarcode suitable for use in the production of a homeopathic remedy.

4. The process of claim 3, further characterized by attenuating said resulting carcode to establish the desired potency thereof.

5. The process of claim 1, wherein said combination is introduced prepartum into the udder of a mammal to effect said conversion therein, and wherein lacteal secretion is withdrawn from the mammal follow parturition.

6. The process of claim 1, wherein said combination is introduced into the udder of a mammal during lactation to effect said conversion therein, and

wherein lacteal secretion is subsequently withdrawn from the mammal.

7. The process of producing a homeopathic product which is characterized by:

A. preparing a first mother from a vaccine that has been inactivated either by heat or chemicals and having a density of McFarland 5, and placing said vaccine in a solution with a vehicle which is non-irritating to tissue;

B. introducing the first mother in an ungulate's udder and effecting conversion of said first mother into a second mother having the characteristics of a sarcode and the homeopathic characteristics of the first mother, and not depending on antibodies;

and

C. removing the second mother from the udder, filtering out larger molecules including antibodies from the second mother with approximately a 0.1 micron filter and serially diluting said second mother.

8. The process of producing a homeopathic product, characterized by introduction into the udder of a mammal an allergenic homeopathic first mother having ei-

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ther toxic or non-toxic or pathogenic or non-pathogenic characteristics, effecting removal in said udder of all dangerous or harmful constituents from said mother and producing lacteal fluid, withdrawing lacteal fluid

from the udder without loss of the desirable homeopathic characteristics of said mother, and not depending on antibodies, separating out and disposing of larger molecules including antibodies from the lacteal fluid which are approximately 0.1 micron and larger, and serially diluting said second mother.

9. The process of claim 8, wherein the initial allergenic substance is an allergen selected from the group consisting of molds, pollens, house dust, fungus, hair, dander, toxins, parasites, microorganisms, bacteria, virus, and sperm.

10. A homeopathic product produced in accordance with the methods as set forth in any one of claims 1 through 8.

11. The process of producing a homeopathic product including the steps of:

A. selecting an allergenic raw material having either toxic or non-toxic or pathogenic or non-pathogenic charac
teristics;

B. creating a solution of such material using a vehicle which is non-irritating to tissue, to produce a homeopathic first mother;

C. introducing the homeopathic mother into a mammal's udder and effecting conversion of the raw product in said solution into an allergenic a second mother having the characteristics of a sarcode and

the homeopathic characteristics of the first mother and not including antibodies;

D. collecting lacteal secretion;

E. establishing the desired potency;

F. filtering out larger molecules including antibodies from lacteal secretion with approximately a 0.1 micron filter;

G. and serially diluting said second mother.

12. The method of producing a mother for use in the production of a homeopathic product including the steps of:

A. selecting an allergenic material having either toxic or non-toxic or pathogenic or non-pathogenic characteristics;

B. creating a solution of such material using a vehicle which is non-irritating to tissue, to produce a homeopathic first mother;

C. introducing the homeopathic mother into an ungulate's udder and effecting conversion of the raw product in said solution into a second mother having the characteristics of a sarcode and the homeopathic characteristics of the first mother and not including antibodies;

D. collecting lacteal secretion;

E. establishing the desired potency;

F. filtering out larger molecules including antibodies from lacteal secretion with approximately a 0.1 micron filter;

G. and serially diluting said second mother.

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Those who are interested in receiving copies of the above may order them from the U.S. Patent Office.

Immunization and usage

There are 3 parts to the process of obtain the basic material for clinic usage

(1) Immunization sequence of cows
(2) Gathering of the colostrum and milk
(3) Packaging of colostral milk

(1) The immunization sequence would start 5 weeks prior to the expected calving date, thus there should be 5 units (vials) of antigen for intra mammary immunization. This intra mammary immunization is identical to a dry cow mastitus treatment but with more sanitation a more complete udder and teat wash and an alcohol cleaning of the teat ends.

Sequence

Immunize
- Most critical
  - 28 days prio to calving
  - 21 "
  - 14 "
  - 7 "
- Not that critical
  - calving

(2) At calving time feed 4 pounds, that would be 2 quarts of the first colostrum to the calf - this is all

the colostrum and mothe melk the calf well receive, the remainder and all the next 5 days (10 meltings) are to be combined. (Remember - cool the melk to ~~room~~ low temperatures prios to combining. Keep cool.

(3) Processing. Mix the melk and colostrum strain thru cheese cloth and put 1 pent in a plastic bag and freeze. Be sure to identify melk
(1) date of packing
(2) Cow identification
(3) Antigen code lot

Keep the melk frozen - It may destabalize on freezing, that is seperate into curds and whey but this, in my testing procedure at the Universty of Minnesota does not effect the protective value.

IV preparation for infected blood to be infused into the cistern

(1) a 3 yr. old pregnant brown Swiss/holstein heifer
(2) udder is disinfected with iodine complex with ethereal and
(3) all utensils are steril
(4) technician wearing plastic med gloves and mask
(5) fresh patient blood infused with teat cannula Jergensen Laboratories Inc., Loveland Colo and syringe
(6) 10 cc 20 days prior to calving
10 cc 15 days prior
10 cc 5 days prior
10 cc 2 days prior
(7) first milk (colastrum) was saved & frozen 24 hrs or approximately 3 gallons was given to patient to thaw and use in daily small quantities.

Herb Saunders Directions

1. Mix 1/3 Impro or Chisholm Colostrum with 2/3 home-made colostrum, if desired.

2. Drink this milk mixture.

3. The cow's first 3 milkings should give 5-6 gallons of milk.

4. Always give the calf 2 pints.

Chisholm Biological Laboratory is 542 Legion Road, Warrenville, SC 29851-9362

Impro Products, Inc. is Waukon, Iowa 52172 (For Veterinarian use only)