Duration of Immunity to Canine and Feline Infectious Disease

- The World Small Animal Veterinary Association states: "We should aim to vaccinate every animal, and to vaccinate each individual less frequently." <u>http://www.wsava.org/SAC.htm</u>
- Age and Long-term Protective Immunity in Dogs and Cats, R.D. Schultz, B. Thiela, E. Mukhtara, P. Sharpa and L.J. Larson, Department of Pathobiological Sciences, School of Veterinary Medicine, University of Wisconsin-Madison:

"Only one dose of the modified-live canine 'core' vaccine (against CDV, CAV-2 and CPV-2) or modified-live feline 'core' vaccine (against FPV, FCV and FHV), when administered at 16 weeks or older, will provide long lasting (many years to a lifetime) immunity in a very high percentage of animals ([Schultz, 1998], [Schultz, 2000] and [Schultz, 2006])."

<u>GUIDELINES FOR THE VACCINATION OF DOGS AND ... - WSAVA</u> www.**wsava**.org/PDF/Misc/**VaccinationGuidelines**2010.pdf

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Vaccination and Misconceptions

Dr Ronald D Schultz, a leading scientists in this field advises:

A significant number of veterinary practitioners believe:

1. The annual revaccination recommendation on the vaccine label is evidence the product provides immunity for (only) one year. Not true.

2. That they are legally required to vaccinate annually and if they don't they will not be covered by liability insurance if the animal develops a vaccine preventable disease - Not true. The only vaccine required at all by law [referring to America] is rabies and even that vaccine is not required in some states. There is also a concern that certain companies will not provide assistance if practitioners don't vaccinate annually with core vaccines. Not true. In fact, all of the major companies have now demonstrated their core products provide at least 3 years of immunity and endorse the "not more often than 3 year" vaccination recommendation made in the AAFP Feline Guidelines and the AAHA Canine Guidelines.

3. That not revaccinating will cause the animal to become susceptible soon (days or a few weeks) after the one year. – Not true for the core vaccines. They provide up to a lifetime of immunity or, at the very least, many years of immunity

4. If the animal is not revaccinated at or before one year the "whole vaccination program needs to be started again". – Not true. If the immune response had been stimulated previously, memory cells will persist well beyond a year for the core vaccines.

5. If they don't continue to revaccinate annually, diseases like canine distemper, canine parvovirus, feline panleukopenia, and infectious canine hepatitis will "reappear and cause widespread disease similar to what was seen prior to the development of vaccines for these diseases." – Not true with the core vaccines. It is not how often you revaccinate; it is dependent on how many animals in the population (herd immunity) receive at least one dose of the core vaccines at an age when MDA cannot block active immunity (eg >16 weeks of age).

6. *That if the revaccination "doesn't help, it won't hurt."* – Not true. Vaccines can and do cause adverse reactions, thus don't administer vaccines if and when they are not needed. Vaccines can cause severe adverse reactions, including death!

7. That giving a vaccine annually that has a duration of immunity of 3 or more years provides much better immunity than if the product is given only once during the three or more years. – Not true.

8. *"It's much cheaper to revaccinate the pet annually than it is to treat the disease the animal will develop because it didn't get revaccinated annually."* This is the "better safe than sorry" philosophy: it is less expensive to prevent disease. This is why it is necessary to use the core vaccines. However, if the core vaccines are given as a puppy and again at 6 months to a year of age, then annual revaccination is not needed. Furthermore, if a vaccine is given that is not needed and it causes an adverse reaction, this is unacceptable and very expensive.

9. They need to revaccinate all new dogs/cats coming to their clinic irrespective of vaccination history even when vaccination records are available from another clinic. Presumably the "other clinic" used the wrong vaccine or didn't know how to vaccinate. – Not true.

10. "Dogs and cats need to be revaccinated annually up to 5 to 7 years of age, then and only then would vaccination every three years be okay." – Not true. Dogs and cats should be vaccinated as puppies and kittens with the core vaccines, making sure the last dose of vaccine is at 14 to 16 weeks of age. They should be revaccinated again at 6 months to 1 year of age, unless titers were performed; then they need not be revaccinated more often than every 3 years. Also, they do not need to have antibody titers performed more often than every 3 years and only then if you decide not to revaccinate.

11. "Surgical procedures, including anaesthesia, are immunosuppressive thus dogs should be vaccinated prior to or shortly after surgery." – Not true. Vaccines should not be given during anaesthesia and animals already vaccinated prior to surgery need not be vaccinated again. If they have never been vaccinated prior to surgery, wait until the animal has recovered from anaesthesia to vaccinate.

12. "Because boarding kennels require annual vaccination, practitioners must continue vaccinating annually with all vaccines." – Not true. Help change kennel rules through education and just use the vaccines that need to be given (e.g. Kennel Cough.) The kennels need to understand that dogs and cats are up-to-date on their core vaccines when they have been vaccinated within the past 5 to 7 years and no kennel should require core vaccines more often than every 3 years.

General Scientific References to Vaccine Adverse Effects

All vaccines come with potential adverse effects. When we vaccinate, we are trading the desire to reduce infectious disease against the known and unknown potential side-effects of vaccines. These side effects include atopy, allergy, autoimmune diseases (including cancer), arthritis, organ failure and neurological effects.

The American Animal Hospital Association (AAHA) Guidelines state:

Do Not Vaccinate Needlessly - Don't revaccinate more often than is needed and only with the vaccines that prevent diseases for which that animal is at risk. They also caution veterinarians: "Do not assume that vaccines cannot harm a patient. Vaccines are potent medically active agents and have the very real potential of producing adverse events."

The American Veterinary Medical Association's (AVMA's) Principles of Vaccination (<u>http://www.avma.org/issues/vaccination/vaccination.asp</u>) states that:

Possible adverse events include failure to immunize, anaphylaxis, immunosuppression, autoimmune disorders, transient infections, and/or long-term infected carrier states. In addition, a causal association in cats between injection sites and the subsequent development of a malignant tumor is the subject of ongoing research.

Dr Ronald D Schultz (2007) provides this list of adverse events known to be induced by vaccines:

Common Reactions:

- Lethargy
- Hair Loss, hair color change at injection site
- Fever
- Soreness, stiffness
- Refusal to eat
- Conjunctivitis
- Sneezing
- Oral ulcers

Moderate Reactions:

- Immunosuppression
- Behavioral changes
- Vitiligo (skin reactions)
- Weight loss (Cachexia)
- Reduced milk production
- Lameness
- Granulomas/Abscesses
- Hives

- Facial Edema (swelling)
- Atopy (hereditary allergies)
- Respiratory disease
- Allergic Uveitis (Blue Eye)

Severe Reactions triggered by Vaccines:

- Vaccine injection site sarcomas (in dogs and ferrets as well as cats)
- Anaphylaxis
- Arthritis, polyarthritis
- HOD hypertrophy osteodystrophy
- Autoimmune Hemolytic Anemia
- Immune Mediated Thrombocytopenia (IMTP)
- Hemolytic disease of the newborn (Neonatal Isoerythrolysis)
- Thyroiditis
- Glomerulonephritis
- Disease or enhanced disease which the vaccine was designed to prevent
- Myocarditis
- Post vaccinal Encephalitis or polyneuritis
- Seizures
- Abortion, congenital anomalies, embryonic/fetal death, failure to conceive

The British Veterinary Medicines Directorate listed the following adverse reactions in its pet vaccine position paper:

- Immune mediated diseases and the association with vaccine reactions have been reviewed by Day (1999, 2006), Pedersen (1999) and the VPC Working Group (2002). Vaccine reactions are generally classified into one of four recognised categories: Type I-IV. The immunological theories behind such reactions would suggest that such adverse events should only occur following an immunological reaction to a previously exposed vaccine antigen, adjuvant, excipient or other production remnants such as bovine serum. However, immune mediated reactions can also follow the administration of a primary dose of vaccine and the exact mechanisms for such a reaction are unknown.
- Type I hypersensitivity reactions involve an immune mediated reaction that releases potent
 inflammatory mediators and other chemicals that trigger an anaphylactic reaction in the affected
 animal. The reactions are usually acute, with the clinical signs appearing within minutes or hours of
 vaccination. Typical signs reported are facial oedema, shock, lethargy, respiratory distress and
 diarrhoea. Severe anaphylactic reactions may result in death. Urticaria (hives), facial oedema and
 anaphylactic shock are specific clinical manifestations of Type I hypersensitivities.
- Type II hypersensitivity reactions involve the binding of the animal's own antibodies to cells or a cell matrix. The formation of auto-immune antibodies is thought to involve a number of complex immunological mechanisms. Secondary immune mediated haemolytic anaemia (IMHA) has been associated with vaccination but may also occur following infection, neoplasia or administration of medications. In this condition, auto-antibodies are produced against the animal's own red blood cells but the immunological mechanism by which vaccines may produce such a response is not yet established. Confirmation of IMHA is dependent on the demonstration of auto-antibodies and, therefore, not all reports of such adverse events can be recorded accurately if confirmatory diagnostic tests have not been performed. For the period 2005-2010, 57 suspect adverse reaction reports of immune mediated reactions were submitted to the VMD. Subsequently only 25 of these reports were attributed to immune mediated reactions. Other clinical manifestations of Type II disease include immune mediated thrombocytopenia (IMTP) (autoantibodies to blood platelets) myasthenia gravis (autoantibodies to muscle nerve receptors) and pemphigus (foliaceous & vulgaris) (auto-antibodies to epidermal proteins).
- Type III hypersensitivity reactions result from the formation of circulating complexes of antigen and antibody that deposit in certain organs or tissues in the body leading to inflammatory reactions and destruction of cells and associated matrix. The deposition of immune complexes usually results in inflammation of the blood vessels. The reaction is dependent on the continued presence of both antibody and antigen with the latter being derived from infection, vaccination, medication or exposure of 'self-antigens' through disease. Infections will inevitably result in the formation of immune-complexes as the body aims to rid itself of a foreign invader. Some examples of well known immune-complexes provide clinical signs such as:

(i) 'Blue Eye' is a well documented manifestation of a Type III reaction following infection with CAV-1 and or administration of some of the early CAV-1 vaccines. Replacement of CAV-1 by CAV-2 vaccines have minimised the risk of such adverse events with just six reports of 'blue eye' reported to the VMD during the period 2005-2010.

(ii) Reactions involving type III immune mediated mechanisms have also been demonstrated following rabies virus vaccination.

(iii) Systemic lupus erythematosus (SLE), a disease characterised by the development of antinuclear antibodies (ANAs).

(iv) Drug-induced arthritis has been reported as a Type III reaction but the evidence of similar vaccine associated immune-mediated syndrome is sparse. The VMD has received two reports of pemphigus associated with vaccination during the last five years.

 Type IV hypersensitivity reactions or "delayed-type hypersensitivity" are cell, rather than antibody, mediated. These diseases are usually relatively slow to develop and are dependent on the cellmediated arm of the immune system.

Dr Jean W Dodds, wrote in US Dog World, March, 1995:

Immune–suppressant viruses of the retrovirus and parvovirus classes have recently been implicated as causes of bone marrow failure, immune-mediated blood diseases, haematologic malignancies (lymphoma and leukaemia), dysregulation of humoral and cell-mediated immunity, organ failure (liver, kidney) and autoimmune endocrine disorders – especially of the thyroid gland (thyroiditis), adrenal gland (Addison's disease) and pancreas (diabetes). Viral disease and **recent vaccination** with single or combination modified live virus vaccines, especially those containing distemper, adenovirus 1 or 2 and parvovirus, are increasingly recognised contributors to immune-mediated blood diseases, bone marrow failure and organ dysfunction.

http://www.dogs4dogs.com/shots.html:

"Although any vaccine, including those your dog has previously gotten without incident, can cause an adverse reaction, vaccines made with *killed* virus, however, are the most adversely reactive. This includes the rabies vaccine, Bordetella, Coronavirus, and Leptospirosis. Why? Because *killed* vaccines contain *adjuvants* (additives that "boost" the immune reaction). Live viruses don't need boosting. Fortunately, with the exception of rabies, these other shots are not recommended for all dogs. Also, they are seldom effective. Don't give them without good reason."

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67. Anna R. Spickler and James A. Roth J Vet Intern Med 2003;17:273–281 Adjuvants in Veterinary Vaccines: Modes of Action and Adverse Effects:

Vaccine adjuvants are chemicals, microbial components, or mammalian proteins that enhance the immune response to vaccine antigens. Interest in reducing vaccinerelated adverse effects and inducing specific types of immunity has led to the development of numerous new adjuvants. Adjuvants in development or in experimental and commercial vaccines include aluminum salts (alum), oil emulsions, saponins, immune-stimulating complexes (ISCOMs), liposomes, microparticles, nonionic block copolymers, derivatized polysaccharides, cytokines, and a wide variety of bacterial derivatives. The mechanisms of action of these diverse compounds vary, as does their induction of cell-mediated and antibody responses. Factors influencing the selection of an adjuvant include animal species, specific pathogen, vaccine antigen, route of immunization, and type of immunity needed.

Extract:

Adverse Effects and Potential Hazards of Adjuvants

When immune responses destroy invading microorganisms, they cause tissue damage and result in some of the clinical signs of illness. Similarly, as agents that enhance immune responses, adjuvants can increase the adverse effects of the vaccine. These adverse effects are influenced by the interactions of the specific adjuvant and antigen.9,20

Systemic, nonspecific adverse effects can include fever, arthritis, uveitis, anorexia, soreness, and lethargy.9,20,21 Theoretically, adjuvants also may increase the probability of autoimmune reactions. Overdoses of IL-2, a cytokine proposed as an adjuvant, have been linked to autoimmune diseases. 22 Autoantibodies have been detected after vaccination with typical canine distemper, rabies, and parvovirus vaccines, and a temporal association has been noted between autoimmune hemolytic anemia and vaccination in dogs.21 Adjuvants also may have specific adverse effects related to their chemical nature. For example, some crude saponin adjuvants can result in hemolysis if injected IV.23

68. Strasser A et al: *Immune modulation following immunization with polyvalent vaccines in dogs*. Vet Immunol Immunopathol 2003 94:113-121.

W. Jean Dodds DVM on vaccine adverse effects:

"I don't really believe my training in veterinary college was adequate with regard to animal vaccination. To be fair to current knowledge, I graduated from veterinary college in Canada in 1964. At that time we understood much less about the molecular aspects of immunology, and the long term medical effects of vaccinations, both beneficial and potentially harmful. We also had fewer infectious diseases to treat and prevent, and hence fewer vaccines for them.

"I was always a clinical research scientist, but colleagues and pet owners would tell me about malaise and illness that appeared shortly after pet animals were vaccinated. This was in addition to the rare case of anaphylaxis induced by vaccination. They spoke about irritability, low-grade or even high fever, anorexia, stiffness, occasional seizure-like episodes. These usually occurred from 2-10 days post-vaccination, sometimes longer (up to 45 days).

"The clinical signs associated with vaccine reactions typically include fever, stiffness, sore joints and abdominal tenderness, susceptibility to infections, neurological disorders and

encephalitis, collapse with autoagglutinated red blood cells and icterus (autoimmune hemolytic anemia) (AIHA), or generalized petechiae and ecchymotic hemorrhages (immune-mediated thrombocytopenia) (ITP).^{1, 2, 4, 7, 8, 12, 13}

"Hepatic enzymes may be markedly elevated, and liver or kidney failure may occur by itself or accompany bone marrow suppression. Furthermore, MLV vaccination has been associated with the development of transient seizures in puppies and adult dogs of breeds or cross-breeds susceptible to immune-mediated diseases especially those involving hematologic or endocrine tissues (e.g. AIHA, ITP, autoimmune thyroiditis). ^{1,7,10} Post-vaccinal polyneuropathy is a recognized entity associated occasionally with the use of distemper, parvovirus, rabies and presumably other vaccines. ^{2, 3, 7} This can result in various clinical signs including muscular atrophy, inhibition or interruption of neuronal control of tissue and organ function, muscular excitation, incoordination and weakness, as well as seizures. ⁷

"Certain breeds or families of dogs appear to be more susceptible to adverse vaccine reactions, particularly post-vaccinal seizures, high fevers, and painful episodes of hypertrophic osteodystrophy (HOD).^{7,9} Vaccination of pet and research dogs with polyvalent vaccines containing rabies virus or rabies vaccine alone was recently shown to induce production of antithyroglobulin autoantibodies, a provocative and important finding with implications for the subsequent development of hypothyroidism.¹⁰

Furthermore, injection site fibrosarcomas have recently been documented in dogs as well as cats, and other cancers such as leukemia have been vaccine-associated." ^{7,18}

"If I was in private practice today, I would only use a conservative puppy or kitten series (2-3 doses only) of vaccines: one before 12 weeks in puppies and 10 weeks in kittens; and a second between 14-16 weeks in puppies and 12-14 weeks in kittens. All vaccines should be 3-4 weeks apart. I would not vaccinate beyond the puppy and kitten series, and I would not worry about income impact, regardless, as our veterinary oath requires that we "do no harm". Judicious use of vaccines is paramount.

"I totally embrace my profession and always have, but the pharmaceutical industry has considerable influence on it; there is a huge marketing effort here – that's their job. We are the ones that need to 'sift' this information appropriately. We, the consumer professionals, have allowed this influence to go unchecked. It's time for senior members of our profession to step up and place controls on the commercial influence upon relatively naive veterinary students and new graduates. This influence is even stronger in the pet food and supplements industry. The government also needs to be more proactive and keep up to date."

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Note:

Dr. Dodds received the D.V.M. degree with honors in 1964 from the Ontario Veterinary College, University of Toronto. In 1965 she accepted a position with the New York State Health Department in Albany and began comparative studies of animals with inherited and acquired bleeding diseases. Her position there began as a Research Scientist and culminated as Chief, Laboratory of Hematology, Wadsworth Center. In 1980 she also became Executive Director, New York State Council on Human Blood and Transfusion Services. This work continued full-time until 1986 when she moved to Southern California to establish Hemopet, the first nonprofit national blood bank program for animals.

From 1965-1986, she was a member of many national and international committees on hematology, animal models of human disease, veterinary medicine, and laboratory animal science. Dr. Dodds was a grantee of the National Heart, Lung, and Blood Institute (NIH) and has over 150 research publications. She was formerly President of the Scientist's Center for Animal Welfare; and Chairman of the Committee on Veterinary Medical Sciences and Vice-Chairman of the Institute of Laboratory Animal Resources, National Academy of Sciences.

In 1974 Dr. Dodds was selected as Outstanding Woman Veterinarian of the Year, AVMA Annual Meeting, Denver, Colorado; in 1977 received the Region I Award for Outstanding Service to the Veterinary Profession from the American Animal Hospital Association, Cherry Hill, New Jersey; in 1978 and 1990 received the Gaines Fido Award as Dogdom's Woman of the Year; and the Award of Merit in 1978 in Recognition of Special Contributions to the Veterinary Profession from the American Animal Hospital Association, Salt Lake City, Utah. In 1984 she was awarded the Centennial Medal from the University of Pennsylvania School of Veterinary Medicine. In 1987 she was elected a distinguished Practitioner of the National Academy of Practice in Veterinary Medicine. In 1994 she was given the Holistic Veterinarian of the Year Award from the American Holistic Veterinary Medical Association. She is an active member of numerous professional societies.

Stephen Blake DVM, holistic veterinarian:

"I emphatically do not believe that I was taught adequately with regard to the vaccine issue. I was taught to believe vaccinations were synonymous with immunization. They are two separate entities.

"I was taught vaccines were safe and it was implied there had been safety studies done on them before they were used on the general public. They are not safe and there have not been any safety studies done on any of them.

"I was taught that if something adverse happens within a few hours after immunization it was related to the vaccines but, if it happened later than that period of time, it had nothing to do with the vaccines. The truth of the matter is vaccines can set up a latent condition that may show up within a few hours or years after immunization.

"I was taught you needed to vaccinate every year to boost animals' immune systems. There are no studies to show that annual boosters are ever indicated or that there is any science to support annual vaccines to boost an animal's immune system. I was never taught that mercury and aluminium hydroxide, which are in the vaccines, can cause cancer, are neurotoxins, and can trigger autoimmune disease.

"When I first went into practice, I noticed some animals developed fevers for a few days, became lethargic, lost their appetites, developed ear infections, seizures, pruritus, UTI, musculoskeletal issues, and behaviour issues after vaccination.

"As time went on, I observed that otitis, UTI, autoimmune disease complexes, gingivitis, allergic dermatitis, IBD, asthma, aggression and phobias, convulsions, paralysis, cancer, chronic conjunctivitis, liver disease, kidney disease, cardiac disease, arthritis, anterior cruciate rupture, hip disease, and corneal lesions can be correlated with vaccine damage.

"Pet guardians are being misinformed. There is no scientific evidence that annual vaccines are needed or indicated.

"I feel there is pressure at all levels of veterinary medicine that we are not to say anything negative about vaccines which would alarm the public and make it harder to sell the vaccine concept. There is no informed consent information presented to the pet owner prior to vaccination because they do not want to alarm the owner and make it difficult to promote vaccines. It has been known for over 20 years that rabies vaccines can cause terminal cancer in the feline and I have yet to meet a client who was informed of this scientific fact by their attending veterinarian. This should be made public to all cat owners prior to rabies vaccine so the owner is aware of the low risk of getting rabies compared to the high risk of getting cancer from the rabies vaccine.

"I love the practice of veterinary medicine with an oath to prevent suffering and do no harm. I do not support my profession's over-use of drugs, chemicals and vaccines as we know them today. I feel my profession needs to be the leader in breaking away from the dangers of these products and show the human medical profession this is not healing. It does cause harm.

"I feel the pharmaceutical industry finances the veterinary schools and the veterinary profession. I feel they are the fox in the hen house that sets policy for the practice of medicine as we know it today in our country.

"The pharmaceutical industry has too much influence in veterinary teaching. Their approach to medicine prevents any other modalities of healing from being available in our veterinary schools. This is done so they have no competition for the pet industry dollars from unpatentable means."

Duration of Immunity

"Many Veterinary practices still recommend vaccinations annually, yet the recommendation for annual vaccination is a practice that was officially started in 1978. That recommendation was made without scientific validation of the need to booster immunity so frequently. In fact, the presence of good humoral antibody levels can block the anamnestic response to vaccine boosters just as maternal antibody blocks the response in some young animals. In other words, if a body has been given its initial vaccine and first year booster, giving another vaccine does not create a stronger immunity. However, the danger of over-vaccinating is a very real risk. (Schultz, Ronald D." *Current and future canine and feline vaccination programs*", Veterinary Medicine, March 1998, p. 243) Dr. Ronald Schultz is one of the leading independent researchers and proponents of vaccinating animals less often. Shultz began researching vaccines more than twenty-five years ago when he noticed the two different vaccination approaches for humans and animals—humans were vaccinated as children and then not again…but animals were vaccinated annually. His research confirms that most animal vaccines, like human ones, create long-term immunity. Shultz emphasizes that while it's critical to stimulate initial immunity in animals when they are young, his work has revealed that many vaccines provide lifelong immunity, making repeated vaccinations after the first year of doubtful value. To compound the situation, Shultz has found that indiscriminate vaccination of adult animals can actually trigger adverse physiological reactions.

In studies Dr. Ron Shultz performed at the University of Wisconsin, 106 dogs vaccinated within the previous one to four years were each given a canine parvovirus booster vaccine. Only one of the 106 dogs showed significant increase in serum antibody titer following the booster. These results demonstrated that revaccination does not automatically enhance antibody levels or improve immunity. What happens is that the vaccine virus is neutralized before it can reach the memory T and B cells. The immunity provided by previous vaccination not only protects against the virulent disease but also prevents response to revaccination. (Wolf Alice, *Vaccines of the Present and Future*, Proceedings of the World Animal Veterinary Congress, Vancouver 2001.)

The term "up-to-date" is only valid if you use the vaccine manufacturers' protocols, which are reflective of the amount of animal testing the vaccine company has actually done with a particular vaccine.

Delayed Vaccine Reactions

Animal studies show delayed reactions to vaccine ingredients. A reaction may occur days, weeks, months or years after an animal or human is exposed to vaccines. (*Food and Drug Administration, 1982* as cited in Kirby, 2005, St. Martins Griffin, New York.)

Viral disease and recent vaccination with single or combination modified live-virus (MLV) vaccines—especially that containing distemper virus, adenovirus 1 or 2, and parvovirus—is an increasingly recognized contributor to immune-mediated blood disease, bone marrow failure, and organ dysfunction. (1-11) Potent adjuvanted killed vaccines, like those for rabies virus, can also trigger immediate and delayed (vaccinosis) adverse vaccine reactions. Beyond immediate hypersensitivity reactions, other acute events tend to occur 24-72 hours afterward, or 7-45 days later in a delayed type immunological response." (1-4, 6-10)

Even more delayed adverse effects include mortality from high-titered measles vaccine in infants, canine distemper antibodies in joint diseases of dogs, and feline and canine injections-site fibrosarcomas." (5, 7)

The increasing antigenic load presented to the host individual by modified-live virus (MLV) vaccines during the period of viremia is presumed to be responsible for the immunological challenge that can result in a delayed hypersensitivity reaction. (2,3,6,7)

The clinical signs associated with vaccine reactions typically include fever, stiffness, sore joints, and abdominal tenderness, susceptibility to infections, neurological disorders and encephalitis, collapse with autoagglutinated red blood cells, and icterus (autoimmune hemolytic anemia—AIHA), or generalized petechiae and ecchymotic hemorrhages (immune-mediated thrombocytopenia—ITP). (1, 2, 4 7, 8, 12, 13) Hepatic enzymes may be markedly elevated, and liver or kidney failure may occur by itself or accompany bone marrow suppression. Furthermore, MLV vaccination has been associated with the development of transient seizures in puppies and adult dogs of breeds or cross-breeds susceptible to immune-mediated diseases, especially those involving hematologic or endocrine tissues (i.e. AIHA, ITP, autoimmune thyroiditis)." (1, 7, 10)

"Post-vaccinated polyneuropathy is a recognized entity associated occasionally with the use of distemper, parvovirus, rabies, and presumably other vaccines." (2, 3, 7) "This can result in various clinical signs including muscular atrophy, inhibition or interruption of neuronal control

of tissue and organ function, muscular excitation, uncoordination and weakness, as well as seizures." (7)

Certain breeds or families of dogs appear to be more susceptible to adverse vaccine reactions, particularly post-vaccinal seizures, high fevers, and painful episodes of hypertrophic osteodystrophy (HOD). (7, 9)

Vaccination of pet and research dogs with polyvalent vaccines containing rabies virus or rabies vaccine alone was recently shown to induce production of antithyroglobulin autoantibodies, a provocative and important finding with implications for the subsequent development of hypothyroidism." (10, 17)

Furthermore, injection site fibrosarcomas have recently been document in dogs as well as cats." (18)

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Vaccines and Immune-Mediated Disease

- "There is a real concern that vaccines may predispose certain genetically susceptible individuals to immune-mediated disease. The more antigens we administer, the higher the potential for hypersensitivity. Type I is IgE mediated; type 2, cytotoxic antibody mediated; type 3, immune-complex mediated; and type 4 cellular mediated. All of these hypersensitivities are natural parts of the immune response, but they cause a certain amount of tissue damage. That damage may occur in the kidney, liver, or as was the case with canine adenovirus 1, in the eye. In many cases it is impossible to show a direct connection between the damage and a vaccine, since it is the accumulation of many antigens over many years that results in clinically evident disease." JAVMA, Vol 207, No 4, August 15, 1995 – Current Concepts, are we vaccinating too much?
- 2. The seventh edition of the Merck Veterinary Manual (1991) states: "Bone marrow suppression with transient (21 day) or chronic/latent erythroid dysplasia, in the presence or absence of thrombocytopenia and neutropenia, Combs' positive haemolytic anaemia, and immune-mediated thrombocytopenia have been associated with (i.e., may prove to be caused by) both retroviral and parvoviral infection in man and other species. Also, modified live parvovirus vaccines in dogs, and killed feline leukaemia virus vaccine are suspects as causes (in genetically susceptible animals) of such haematological diseases."
- 3. In Practice, Vol 20 No 2, Feb 1998: Michael Day, senior lecturer in Veterinary Pathology at the University of Bristol states that "environmental influences are crucial to the expression of immune mediated disease and that the most important of these is likely to be exposure to microbial antigens following natural infection or vaccination. Mr Day divides immune mediated disease into four main groups hypersensitivity diseases, autoimmune diseases, immune system neoplasia [tumour formation] and immunodeficiency diseases".
- 4. In a letter to Veterinary Times during July 1999, veterinarian Lyn Thomson responded, "This would indicate that veterinarians must consider and report the whole range of immune mediated diseases post vaccination, including flea allergy, atopic dermatitis, dietary hypersensitivity, contact hypersensitivity, asthma, autoimmune diseases, lymphoma, lymphoid leukaemia, multiple myeloma, plasmcytoma, hisiiocytoma, thymoma, and immunodeficiency disease."
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- 7. In 2000, research showed that **polyarthritis and other diseases like amyloidosis in dogs were linked to combined MLV vaccines** (Am Coll Vet Intern Med, 2000; 14: 381).
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- http://wvc.omnibooksonline.com/ data/papers/2010_V127.pdf : The effects of contaminated feline vaccines. Vaccine Induced Antibodies Against Feline Tissues Michael R. Lappin, DVM, PhD, DACVIM The Kenneth W. Smith Professor in Small Animal Clinical Veterinary Medicine, College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins, CO, USA
- 10. Dr Ronald Schultz, Vet Med Today (JAVMA Vol 207, No 4, August 15, 1995): *"Immune-mediated disease has developed in human beings following vaccination, as was seen with cases of Guillain-Barre syndrome following swine flu vaccinations, and rheumatoid arthritis following influenza vaccination".*
- 11. Med Hypotheses, Waisbren BA Sr, 2008;70(2):346-8. Epub 2007 Jul 13. Acquired autoimmunity after viral vaccination is caused by molecular mimicry and antigen complimentarity in the presence of an immunologic adjuvant and specific HLA patterns.
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- 19. L. Tomljenovic and C.A. Shaw, *Aluminum Vaccine Adjuvants: Are they Safe?* Current Medicinal Chemistry, 2011, *18*, 2630-2637 "Aluminium presented in this form carries a risk for autoimmunity, long-term brain inflammation and associated neurological complications and may thus have profound and widespread adverse health consequences."
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- 22. Lappin MR, et al: Investigation of the induction of antibodies against Crandall-Ress feline kidney cell lysates and feline renal cell lysates after parenteral administration of vaccines against feline viral rhinotracheitis, calicivirus and panleukopenia in cats. Am J Vet Res 2005 66: 506-511.
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Vaccines and Atopy

- 1. Frick OL, Brooks DL. *Immunoglobulin E antibodies to pollens augmented in dogs by virus vaccines*. Am J Vet Res 44: 440, 1981.
- 2. An augmented immune response to vaccination is seen in dogs with pre-existing inhalant allergies (i.e., atopy) to pollens. Furthermore, the increasing current problems with allergic and immunological diseases have been linked to the introduction of MLV vaccines more than 20 years ago. While other environmental factors no doubt have a contributing role, the introduction of these vaccine antigens and their environmental shedding may provide the final insult that exceeds the immunological tolerance threshold of some individuals in the pet population. (Tizard 1. *Risks associated with use of live vaccines.* J Am Vet Med Assoc 1990;196:1851-1858.) (Dodds WJ. *More bumps on the vaccine road.* Adv Vet Med 1999; 41: 715-732.)
- 3. <u>http://veteriner.fusabil.org/pdf/pdf_FUSABIL_604.pdf</u> Acute Angioedema Following Immunization Against Parvovirus in a German Shepherd Dog and Clinical Remission With Treatment
- 4. Familial predisposition to atopy is reflected in the Merck Manual which advises that a child with, or from a family with, B and/or T cell immunodeficiencies should not receive live virus vaccines due to the risk of fatality. Merck states: "Features of B cell deficiencies include respiratory or food allergies; features of T cell deficiencies include heart disease; and features of combined T and B cell deficiencies include dermatitis, neurological deterioration and eczema."
- 5. "Multiple vaccinations shift this delicate balance [between Th1 and Th2], favoring the development of atopy and, perhaps, autoimmunity through vaccine-induced polyclonal activation leading to autoantibody production. An increase in the incidence of childhood atopic diseases may be expected as a result of concurrent vaccination strategies that induce a Th2-biased immune response. What should be discussed is whether the prize of a reduction of common infectious diseases through a policy of mass vaccination from birth is worth the price of a higher prevalence of atopy." http://vran.org/health-risks/anaphylaxis-allergies-and-asthma/multiple-vaccination-effects-on-atopy/
- 6. There is a correlation between hypothyroidism and IgA and IgM deficiency http://www.ncbi.nlm.nih.gov/pubmed/15925836
- 7. "Expression and characterization of a low molecular weight recombinant human gelatin: development of a substitute for animal-derived gelatin with superior features."
 "Gelatin is used as a stabilizer in several vaccines. Allergic reactions to gelatins have been reported, including anaphylaxis. These gelatins are derived from animal tissues and thus represent a potential source of contaminants that cause transmissible spongiform encephalopathies." Olsen D, et al, Protein Expr Purif.; 40(2):346-57 -- 4/1/2005
- 8. Professor Tara Shirakawa, published the results of a Japanese study on 867 infants who received BCG vaccine. Thirty-six percent developed allergies. The number of

TB cases in the province didn't increase, but the incidence of severe allergy did. (Science, vol 275, 3 Jan 1997)

- 9. A number of studies have linked atopic dermatitis in humans to vaccines, specifically the measles, mumps and rubella vaccine, measles infection, and the BCG (tuberculosis) shot <u>http://www.ncbi.nlm.nih.gov/pubmed/14690341</u>, <u>https://www.escholar.manchester.ac.uk/uk-ac-man-scw:104044</u>
- 10. Pediatric Allergy & Immunology (19 (1): 46-52, February 2008), looked at the potential causal factor in the development of **atopic disease due to the effect of pertussis immunization on specific IgE antibodies.** All associations between vaccination and atopic disorders were positive. The report concluded: "*Egg-related allergy is common, particularly in children with asthma or general allergies, and may be as high as 40% in children with atopic dermatitis. The risk of egg-related allergy after vaccination depends on the presence of egg protein in the final product."*
- 11. Allergy 1978, Jun:33(3):155-9 reported that *aluminium phosphate stimulates the IgE response in guinea pigs to tetanus toxoid.* "It is hypothesized that the regular application of aluminium compound-containing vaccines ... could be one of the factors leading to the observed increase of allergic diseases."
- 12. In Pediatr Allergy Immunol 1994 May;5(2):118-23, the role of aluminium for IgG and IgE responses to pertussis toxin, as well as side effects, was investigated in 49 children with known atopy status. The addition of aluminium to pertussis vaccine was associated with strong IgG antibody response, and a stronger IgE antibody response. The study concluded that the role of immunization in the development of allergy merits further studies.
- <u>http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2998561/</u> looks at the role of IgE antibodies in atopic dermatitis and refers to post-vaccination specific IgE responses to tetanus and diphtheria toxoid, which could result in adverse events to future vaccination or exposure to the diseases.
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- Petrik MS, Wong MC, Tabata RC, Garry RF, Shaw CA (2007). *Aluminum adjuvant linked to gulf war illness induces motor neuron death in mice*. Neuromolecular Med 9 (1): 83–100. <u>doi:10.1385/NMM:9:1:83</u>. <u>PMID 17114826</u>
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- 20. Exley, C.; Swarbrick, L.; Gherardi, R.K.; Authier, F.J. *A role for the body burden of aluminium in vaccine-associated macrophagic myofasciitis and chronic fatigue syndrome.* Med Hypotheses. 2009, *72*(2), 135-139.
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- 22. Ohmori K et al: *IgE reactivity to vaccine components in dogs that developed immediate-type allergic reactions after vaccination.* Vet Immunol Immunopathol 2005 104:249-256.
- 23. Vitale CB, Gross TL, Magro CM: *Vaccine-induced ischemic dermatopathy in the dog.* Vet Dermatol 1999 10:131-142.

Neurological effects of vaccines

- Encephalitis has been shown to appear in dogs after vaccination. (Grene, CE, ed, Appel MJ, Canine Distemper in Infectious Diseases of the Dog and Cat, 2nd edition, Philadelphia: WB Saunders, 1998: 9-22).
- Veterinary Record 1992 (130, 27-30), AIP McCandlish et al: "Post-vaccinal encephalitis is a recognised complication of the administration of certain strains of live attenuated canine distemper vaccine (Hartley 1974, Bestetti and others 1978, Cornwell and others 1988)".
- 3. Braund's Clinical Neurology in Small Animals: Localisation, Diagnosis and Treatment:

"Post vaccinal canine distemper encephalitis occurs in young animals, especially those less than six months of age. It has been recognised as a disease entity for a number of years, and is believed to be association with vaccination using live virus. The pathogenesis of this disease is unclear, but may result from insufficient attenuation of the vaccine virus which causes subsequent infections of the CNS; the triggering of a latent distemper infection by vaccination; other vaccine components; or an enhanced susceptibility of the animal (e.g., animals that are immunosuppressed)."

- Encephalitis following vaccination against distemper and infectious hepatitis in the dog. "A 4-months-old, male, healthy dog developed CNS-symptoms 10 days after the second vaccination with live, attenuated distemper and canine hepatitis virus." G. Bestetti1, et al, Acta Neuropathologica Volume 43, Numbers 1-2 / 69-75 -- 1/1/1978
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- 6. Protein glutamate is added to vaccines to preserve the virus in vaccines. Meat, fish eggs, milk and cheese tend to be high in protein glutamate. High levels of glutamic acid have been shown in animal studies to cause damage to parts of the brain unprotected by the blood-brain barrier, leading to a variety of chronic diseases http://www.ncbi.nlm.nih.gov/pubmed/15167034
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- 8. "Clinical picture of postvaccinal encephalitis after rabies vaccination and sequelae." Uchimaura Y, et al, Nervenarzt; 29(7): 303-7. -- 7/1/1958
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to neural antigens in 36 patients with major neurologic complications, 25 with minor complications, and 39 with no complications after immunization with a brain-derived, Semple rabies vaccine." T Hemachudha, et al, New England Journal of Medicine Volume 316:369-374, Number 7 -- 2/12/1987

- Risks of convulsion and aseptic meningitis following measles-mumps-rubella vaccination in the United Kingdom. "Measles-mumps-rubella (MMR) vaccines containing the Urabe strain of mumps were withdrawn in the United Kingdom in 1992 following demonstration of an increased risk of aseptic meningitis 15-35 days after vaccination. Following introduction of a replacement MMR vaccine (Priorix)... an elevated relative incidence of convulsion was found in the 6- to 11-day period after receipt of Priorix." Miller E, et al, Am J Epidemiol.;165(6):704-9. -- 3/15/2007
- 11. Neurological adverse events associated with vaccination: "These complications include autism (measles vaccine), multiple sclerosis (hepatitis B vaccine), meningoencephalitis (Japanese encephalitis vaccine), Guillain-Barre syndrome and giant cell arteritis (influenza vaccine), and reactions after exposure to animal rabies vaccine. Seizures and hypotonic/hyporesponsive episodes following pertussis vaccination and potential risks associated with varicella vaccination, as well as vaccine-associated paralytic poliomyelitis following oral poliovirus vaccination, are also described." Piyasirisilp, Sucheep a; Hemachudha, Thiravat b, Neurology. 15(3):333-338 -- 6/1/2002
- Acute disseminated encephalomyelitis: "T cell mediated autoimmune response to myelin basic protein, triggered by an infection or vaccination, underlies its pathogenesis " R K Garg, Postgraduate Medical Journal; 79:11-17 -- 1/1/2003
- 13. Neurologic complications of immunization. "Individual vaccines can produce systemic or neurologic reactions ranging from minor events, such as pain and erythema at the injection site, to major complications, such as seizures, shock, encephalopathy, or death." Bale JF Jr, J Child Neurol.; 19(6): 405-12. -- 6/1/2004
- 14. Merck: "In acute disseminated encephalomyelitis (post infectious encephalitis), demyelination can occur spontaneously, but usually follows a viral infection or inoculation (or very rarely a bacterial vaccine), suggesting an immunologic cause."
- 15. "Expression and characterization of a low molecular weight recombinant human gelatin: development of a substitute for animal-derived gelatin with superior features." "Gelatin is used as a stabilizer in several vaccines. Allergic reactions to gelatins have been reported, including anaphylaxis. These gelatins are derived from animal tissues and thus represent a potential source of contaminants that cause transmissible spongiform encephalopathies." Olsen D, et al, Protein Expr Purif.; 40(2):346-57 -- 4/1/2005
- 16. Ballerini, Rico B et al., *Neurological Complications of Vaccination With Special Reference to Epileptic Syndrome* Riview Neurol, Jul-Aug 1973; 43: 254-258.
- 17. Toxicol Environ Chem 2008 90(5):997-1008, researchers found a *correlation between the Hepatitis B triple series vaccine and developmental disability in US children aged 1-9 years*
- 18. Perl, D.P.; Moalem, **S.** *Aluminum and Alzheimer's disease, a personal perspective after 25 years.* J Alzheimers Dis. 2006, *9*(3 Suppl), 291-300.
- 19. Wisniewski, H.M.; Sturman, J.A.; Shek, J.W. *Chronic model of neurofibrillary changes induced in mature rabbits by metallic aluminum*. Neurobiol Aging. 1982, *3*(1), 11-22.
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- 25. Walton, J.R.; Wang, M.X. *APP expression, distribution and accumulation are altered by aluminum in a rodent model for Alzheimer's disease.* J Inorg Biochem. 2009, *103*(11), 1548-1554.
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- 29. Cohly, H.H.; Panja, A. *Immunological findings in autism.* Int Rev Neurobiol.2005, *71*, 317-341.
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- 31. *Aluminum Vaccine Adjuvants: Are they Safe?* L. Tomljenovic, and C.A. Shaw, Current Medicinal Chemistry, 2011, *18*, 2630-2637 "Aluminium presented in this form carries a risk for autoimmunity, long-term brain inflammation and associated neurological complications and may thus have profound and widespread adverse health consequences."
- 32. Department of Paediatrics, Tokyo Medical University, Japan, found the measles virus in patients with inflammatory bowel disease and autism. (Dig Dis Sci, 2000, Apri; 45(4) 723-9). The sequences obtained from the patients with ulcerative colitis and children with autism were consistent with vaccine strains. It should be remembered that the measles virus and canine distemper are very closely related.
- "Neurologic complications of smallpox vaccine" "A variety of neurologic complications of smallpox vaccination have been reported, including encephalitis, transverse myelitis, meningitis, and polyneuritis" Lanska, D, Meldink.com: Neurology --1/1/1900
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- 35. The Journal of the American Medical Association on April 2, 1937: **"A multiplicity of untoward sequelae have been observed in patients treated with immune serum**...The common symptomatology includes fever, urticaria, erythema, oedema, lymphadenoma, artharaliga, smothering sensations, headache, nausea and vomiting. Occasionally there are more serious and lasting manifestations such as peripheral neuritis, epididymitis and orchitis."
- 36. "The Smallpox Vaccine and Postvaccinal Encephalitis" "Before we become complacent with the idea that we will respond to a bioterrorism attack with a mass immunization program for smallpox, it is important to be reminded of the risk and clinical manifestations of postvaccinal encephalitis... The first case of postvaccinal encephalitis as a complication of the Jennerian cowpox inoculation was observed in 1905. A century later, there is no effective therapy." Karen L. Roos, et al, Semin Neurol 22: 095-098 -- 1/1/2002
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- "Coincidence of virus encephalitis and measles-mumps vaccination" "A 15-monthold girl developed meningoencephalitis 7 days after measles/mumps vaccination, and died 3 days later. " Jorch, G. et al, Monatsschr Kinderheilkd 1984; 132(5):299-300 --1/1/1900
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- 42. *"Etiology of acute encephalomyelitis after rabies vaccination."* Piskareva NA, Vopr Virusol; 1(6):47-50. -- 11/1/1956
- 43. **"Experimental studies on paralysis after antirabies vaccination.** Histological studies on acute demyelinating encephalomyelitis in guinea pigs. Shiina T, et al, Jpn J Microbiol; 2(2):187-96. -- 4/1/1958
- 44. "Clinical picture of postvaccinal encephalitis after rabies vaccination and sequelae." Uchimaura Y, et al, Nervenarzt; 29(7): 303-7. -- 7/1/1958
- 45. **"Transient cerebellar ataxia following the administration of attenuated oral antipoliomelitis vaccine (Sabin types II and III).**" Colarizi A, et al, Riv Ist Sieroter Ital.; 38:1-12. -- 1/1/1963
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- 47. "Multiple sclerosis and vaccination." Miller H, et al, Br Med J.; 2(5546): 210-3. --4/1/1967

- 48. **"The management of meningoencephalitis following rabies vaccination"** Klemm D, et al, Med Klin;63(34):1354. -- 8/1/1968
- 49. *"Further Studies of a Simian Virus 40-Like Virus Isolated from Human Brain"*"A virus similar to simian virus 40 was reisolated from brain homogenates of a patient with progressive multifocal leukoencephalopathy onto cultures of human fetal brain cells."
 L. P. Weiner, J Virol.;10(1): 147-149 -- 7/1/1972
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Vaccines and Diabetes

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