

# Vaccine components and constituents: responding to consumer concerns

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The World Health Organization states “The two public health interventions that have had the greatest impact on the world’s health are clean water and vaccines”.<sup>1</sup> However, rates of vaccination uptake in Australia may be suboptimal.<sup>2,3</sup> Concern about vaccine safety is a potential barrier to immunisation; and reductions in vaccination rates have been described after media reporting of adverse effects.<sup>4</sup>

Vaccination safety is a frequent motivation for consumers to contact drug information services operating out of the Mater Health Services in Brisbane (personal reflection). Vaccines contain constituents such as preservatives, stabilisers, adjuvants and biological growth media, which may contribute to consumer concern about vaccine safety; specifically:

- presence of preservatives;
- likelihood of allergic reactions; and
- constituents of human or animal origin.

Community-based health professionals are in a key position to address these concerns by providing accurate information about vaccine constituents and components. However, much of this information is not readily available. We sought to compile a comprehensive overview of constituents, culture and growth media used in the production of the vaccines available in Australia.

## Information retrieval

Information was retrieved using the following iterative process:

- The Therapeutic Goods Administration (TGA) website was used to ascertain vaccines registered in Australia.
- Manufacturers were contacted to confirm current products.
- This was compared with the Australian Immunisation Handbook to ensure all products were included.
- Information about excipients and media was obtained from registered Product Information.
- Where clarification of constituents was required, manufacturers were contacted.
- Final table sections were submitted to individual manufacturers for review.

Information is presented in two tables: childhood vaccines (Box 1) and travel vaccines (Box 2). As vaccine manufacture is subject to ongoing development and change, information provided in this review is current at the time of preparation.

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## ABSTRACT

- Vaccination remains a vital strategy in the prevention of infectious disease.
- Commercial vaccine formulations contain a range of additives or manufacturing residuals, which may contribute to patient concerns about vaccine safety.
- Primary health care professionals are well placed to address patient concerns about vaccine safety. We describe the key constituents present in vaccines, discuss issues related to safety and acceptability of these constituents, and provide a table highlighting constituents of commercially available vaccines in Australia.

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## Preservatives

### Thiomersal

Thiomersal (sodium ethylmercuric thiosalicylate) is an organic compound containing ethylmercury that has been widely used as a vaccine preservative since the 1930s. Concerns have focused on its potential toxicity as a heavy metal, and its role in the claimed link between measles, mumps and rubella (MMR) vaccination and autism.<sup>5</sup>

A recent study assessed whether multiple vaccinations can lead to mercury accumulation.<sup>6</sup> In full-term infants exposed to vaccines containing thiomersal, mercury concentrations detected in blood (range, 2.85–20.55 nmol/L) were well below the level thought to be associated with adverse effects. Additionally, ethylmercury appears to be eliminated via the gastrointestinal tract soon after exposure (estimated half-life, 7 days).<sup>6</sup> Because the developing fetus and low birthweight babies are more vulnerable to toxic effects of mercury, it has been suggested that exposure to vaccines containing thiomersal at time of birth may pose some risk in very low birthweight premature infants.<sup>6</sup> To minimise any potential risk, all vaccinations in the Australian Standard Vaccination Schedule for children younger than 5 years are now thiomersal-free or contain only trace amounts.<sup>7</sup>

In 1998, a case series was published describing 12 children with pervasive development disorder with gastrointestinal features.<sup>8</sup> The report claimed that exposure to MMR vaccination may have been linked to emergence of behavioural symptoms. Since then, controversy has surrounded the potential association between MMR vaccine and autism, with thiomersal a suggested culprit. The original claims have been criticised for being based on uncontrolled, anecdotal associations, and more recently, some of the study authors have retracted their interpretation associating MMR vaccines with autism.<sup>9</sup> Larger epidemiological studies have also failed to demonstrate an association between MMR vaccination or use of thiomersal-containing vaccines and autism.<sup>10</sup>

The mercury or thiosalicylate components of thiomersal may produce hypersensitivity reactions.<sup>11</sup> Reactions are uncommon, even in those with sensitisation, and serious reactions are rare.

## 1 Childhood vaccines

Generic	Vaccine	Live vaccine	Biological growth media	Cells	Other additives
Chicken pox ( <i>Varicella</i> )	Varilrix (GSK)	Y	Cow, human	Human cell culture	Neomycin, lactose
	Varivax — refrigerated (MSD)	Y	Gelatine, cow	Human and guinea pig cell culture	Neomycin, monosodium glutamate
Diphtheria/ tetanus	ADT (CSL); CDT (CSL)	N	Cow or pig or horse*	Biological culture	Thiomersal, aluminium phosphate
Diphtheria/ tetanus/ pertussis	Boostrix (10 years) (GSK)	N	Cow	Biological culture	Formaldehyde, phenoxyethanol, aluminium phosphate, aluminium hydroxide
	Infanrix (GSK)	N	Cow	Biological culture	Formaldehyde, phenoxyethanol, aluminium hydroxide
	Tripacel (Aventis Pasteur)	N	—	Biological culture	Phenoxyethanol, aluminium phosphate
Diphtheria/ tetanus/ pertussis/ hepatitis B	Infanrix Hep B (GSK)	N	Cow	Yeast (hep B), biological culture	Formaldehyde, phenoxyethanol, aluminium phosphate and hydroxide
Diphtheria/ pertussis/ poliomyelitis/ tetanus	Infanrix IPV (GSK)	N	Cow	Monkey cell culture, biological culture	Formaldehyde, neomycin, phenoxyethanol, aluminium hydroxide, polymyxin B
Diphtheria/ hepatitis B/ pertussis/ poliomyelitis/ tetanus	Infanrix Penta (GSK)	N	Cow	Yeast (hep B), monkey cell culture, biological culture	Formaldehyde, neomycin, phenoxyethanol, aluminium phosphate and hydroxide, polymyxin B
Diphtheria/ <i>Haemophilus influenzae</i> / hepatitis B/ pertussis/ poliomyelitis/ tetanus	Infanrix Hexa (GSK)	N	Cow	Yeast (hep B), monkey cell culture, biological culture	Formaldehyde, neomycin, phenoxyethanol, lactose, aluminium phosphate and hydroxide, polymyxin B
Diphtheria toxoid	Diphtheria Vacc (Adsorbed) (CSL); Diphtheria Vacc (Adsorbed) (Adult) (CSL)	N	Cow or pig or horse*	Biological culture	Thiomersal, aluminium phosphate
<i>Haemophilus influenzae</i> type B	Liquid Pedvax HIB (MSD)	N	—	Biological culture	Aluminium hydroxide
<i>Haemophilus influenzae</i> type B with hepatitis B	Comvax (MSD)	N	—	Biological culture, yeast	Aluminium hydroxide
Hepatitis B	Engerix - B (GSK); Engerix-B (Paediatric) (GSK)	N	Cow	Yeast	Thiomersal, aluminium hydroxide
	H-B Vax II (MSD); H-B Vax II Dialysis (MSD); H-B Vax II (Paed) (MSD)	N	—	Yeast	Formaldehyde, aluminium hydroxide, potassium thiocyanate
	Fluad (Chiron)	N	Chicken, egg	—	Formaldehyde, neomycin, squalene (shark liver oil), kanamycin sulfate
Influenza	Fluarix (GSK)	N	Cow, egg	Hen's egg cell culture	Formaldehyde, thiomersal, gentamicin
	Fluvax (CSL)	N	Egg	—	Neomycin, polymyxin B
	Influvac (Solvay)	N	Egg	—	Gentamicin
	Vaxigrip (Aventis Pasteur); Vaxigrip Junior (Aventis Pasteur)	N	Egg	—	Thiomersal in batches manufactured before February 2005 Formaldehyde, neomycin
Measles/ mumps/ rubella	M-M-R II (MSD)	Y	Gelatine, cow	Human cell culture, chick embryo cell culture	Neomycin, human serum albumin
Meningococcal C	Priorix (GSK)	Y	Cow, egg	—	Neomycin, lactose
	Meningitec (Wyeth)	N	Cow (milk)	Biological culture, yeast	Aluminium phosphate, diphtheria conjugate
	Menjugate (CSL)	N	Cow	Biological culture	Aluminium hydroxide, diphtheria conjugate
	NeisVac-C (Baxter)	N	Cow	Biological culture	Aluminium hydroxide, tetanus conjugate
Pneumococcal	Pneumovax 23 (MSD)	N	Rabbit	Biological culture	Phenol
	Prevenar (Wyeth)	N	Cow (milk)	Biological culture, yeast	Aluminium phosphate, diphtheria conjugate
Poliomyelitis	Ipol (Aventis Pasteur)	N	Cow	Monkey cell culture	Formaldehyde, neomycin, streptomycin, polymyxin B
	Polio Sabin (GSK)	Y	Cow	Human cell culture	Neomycin, polymyxin B
Rubella	Meruvax II (MSD)	Y	Gelatine, cow	Human cell culture	Neomycin, human serum albumin
Tetanus	Tet-Tox (CSL)	N	Cow or pig or horse*	Biological culture	Thiomersal, aluminium phosphate

\* These vaccines may contain serum from any one of these sources. This differs from batch to batch and the manufacturer would need to be contacted for information about a specific batch. Biological culture = culture of unspecified source or source may vary between batches. GSK = GlaxoSmithKline. MSD = Merck, Sharp and Dohme. Y = yes. N = no. ◆

2 Travel vaccines		Live vaccine	Biological growth media	Cells	Other additives
Cholera ( <i>Vibrio cholerae</i> )	Dukoral (Aventis Pasteur)	N	—	Biological culture	Formaldehyde
Hepatitis A	Avaxim (Aventis Pasteur); Havrix Junior (GSK); Havrix 1440 (GSK)	N	Cow	Human cell culture	Formaldehyde, neomycin, phenoxyethanol, aluminium hydroxide
	VAQTA Adult (MSD); VAQTA Paediatric/Adolescent (MSD)	N	Cow	Human cell culture	Formaldehyde, aluminium hydroxide
Hepatitis A and hepatitis B	Twinrix 720/20 (GSK); Twinrix Junior 360/10 (GSK)	N	Cow	Human cell culture, yeast (hep B)	Formaldehyde, neomycin, phenoxyethanol, aluminium phosphate and hydroxide
Hepatitis A and <i>Salmonella typhi</i>	Vivaxim (Aventis Pasteur)	N	Cow	Human cell culture	Formaldehyde, neomycin, phenoxyethanol, aluminium hydroxide
Japanese encephalitis	Je-Vax (Aventis Pasteur)	N	Gelatin	Live mice	Formaldehyde, thiomersal, monosodium glutamate
Meningococcal	Menomune (Aventis Pasteur)	N	Cow	Biological culture	Lactose
	Mencevax ACWY (GSK)	N	Cow	Biological culture	Lactose, phenol
Plague ( <i>Yersinia pestis</i> )	Plague Vaccine (CSL)	N	Cow, pig or horse	Biological culture	Phenol
Q fever ( <i>Coxiella burnetii</i> )	Q-Vax (CSL)	N	Egg	—	Formaldehyde, thiomersal
Rabies	Mérieux Inactivated Rabies Vaccine (Aventis Pasteur)	N	Cow	Human cell culture	Neomycin, β-propiolactone, human serum albumin
Tuberculosis	BCG Vaccine (Aventis Pasteur)	Y			
Typhoid ( <i>Salmonella typhi</i> )	Typhim VI (Aventis Pasteur); Typherix (GSK)	N	Cow	Biological culture	Phenol
Typhoid oral ( <i>Salmonella typhi</i> )	Typh-Vax Oral (CSL) (discontinued)	Y	Gelatin	Biological culture	Lactose
Yellow fever	Stamaril (Aventis Pasteur)	Y	Cow, egg	—	Lactose

Biological culture = culture of unspecified source or source may vary between batches. GSK = GlaxoSmithKline. MSD = Merck, Sharp and Dohme. Y = yes. N = no. ♦

**Phenoxyethanol**

2-Phenoxyethanol is an alternative to thiomersal. One report describes generalised eczema occurring after vaccination where 2-phenoxyethanol was found to be the sensitising agent.<sup>12</sup>

**Antibiotics**

Antibiotics such as neomycin and polymyxin B are often used to prevent bacterial contamination during vaccine manufacture;<sup>5</sup> they may contribute to systemic allergic reactions, including anaphylaxis, or local skin reactions.<sup>13</sup> Previous skin reactions to neomycin are not considered a risk factor for anaphylaxis and are not a contraindication for use of neomycin-containing vaccines.<sup>13</sup> Neomycin concentrations may vary between vaccines, but most contain only residual amounts.<sup>14</sup>

**Aluminium**

Adjuvants are used in vaccine manufacture to enhance immune responses to the vaccine antigen. Aluminium hydroxide and phosphate are commonly used adjuvants, and can augment type 2 (antibody-mediated) immune responses without influencing type 1 (cell-mediated) immune responses, or cytotoxic T cell responses.<sup>15</sup> Aluminium adjuvants also induce antigen-specific IgE responses, which may predispose vulnerable individuals to allergic reactions. However, no data were identified associating use of aluminium adjuvants with increased risk of allergy-related events.

Because higher dose exposure to aluminium salts can be toxic, guidelines have been developed for safe levels of exposure. Exposure to aluminium from vaccines is lower than intake from

diet or medications such as antacids,<sup>7</sup> and is well below the current minimum risk level of 2.0 mg/kg per day.<sup>16</sup>

The presence of aluminium adjuvants has been associated with injection-site reactions such as nodules, granulomas and erythema.<sup>17,18</sup> A systematic review of controlled safety studies reported that vaccines containing aluminium produce more erythema and induration than other vaccines in young children (up to 18 months of age), and greater local pain in older children (10–18 years).<sup>19</sup> No association was found between aluminium and more serious or long-term adverse effects.

It has been proposed that use of aluminium adjuvants may lead to the syndrome macrophagic myofasciitis, a histological finding where aluminium-containing macrophages infiltrate muscle tissue, and may be accompanied by a clinical syndrome of myalgia, arthralgia and fatigue.<sup>20</sup> There are about 100 published cases of this syndrome, most from France. As no controlled studies of this potential adverse effect have been conducted, a causal relationship with use of aluminium containing vaccine has not been demonstrated.<sup>20</sup>

**Biological growth media, additives and cells**

**Gelatin**

Gelatin is a partially hydrolysed collagen, usually of bovine or porcine origin, and is one of many types of stabilisers added to vaccines.<sup>5</sup> It may be responsible for some allergic reactions occurring after vaccination, with symptoms including urticaria, anaphylaxis, or local reactions.<sup>21</sup> “Egg allergies” reported after MMR vaccination were found to occur in individuals with no

sensitivity to egg,<sup>5</sup> and were later found to represent gelatin sensitivity. However, the incidence of anaphylaxis to gelatin is low (about one case per 2 million doses).<sup>5</sup>

### Chick embryos and eggs

Egg-related allergy is common, particularly in children with asthma or general allergies, and may be as high as 40% in children with moderate to severe atopic dermatitis.<sup>21</sup> The risk of egg-related allergy after vaccination depends on the presence of egg protein in the final product. For example, influenza vaccine is manufactured using the extra-embryonic fluids of chick embryos and contains measurable quantities of egg proteins.<sup>21</sup> Although the National Health and Medical Research Council (NHMRC) immunisation guidelines state that “individuals with anaphylactic hypersensitivity to eggs should not be given influenza vaccine”,<sup>7</sup> little evidence is available to identify the actual risk of serious allergic reactions in this context. In fact, one study reported that graded dosing of influenza vaccine in 27 patients with a history of anaphylactic reactions to egg ingestion was well tolerated and not associated with significant allergic reactions.<sup>22</sup> Current guidelines and evidence suggest that patients with egg allergies, other than anaphylaxis, may be vaccinated safely.<sup>7,22,23</sup>

MMR vaccine is developed using chick embryo fibroblast tissue, and the final commercial vaccine does not contain egg proteins. Egg allergy is not a contraindication;<sup>7</sup> previous reports of allergy-related adverse events occurring after MMR vaccination have now been attributed to the presence of gelatin.<sup>5</sup>

### Animal and human sera

Vaccine manufacture requires the production of organisms cultivated on an appropriate culture medium. A medium must provide nutrients such as proteins, albumin, polypeptides, and growth factors specific to the needs of the microbe. Animal sera are frequently added to culture media to provide nutrients for microbial growth. Bovine serum is primarily used, although serum from pigs, horses, rabbits or humans may also be used.<sup>24</sup> Extensive filtering processes ensure that the final vaccine contains little, if any, of the original cell material. Some media are serum-free or may be of synthetic, semi-synthetic or yeast origin.

### Yeast

Some vaccines are manufactured using *Saccharomyces cerevisiae* (baker's yeast). There are no reports of yeast-specific IgE detected in patients following exposure to vaccines manufactured using baker's yeast. Currently, the risk of vaccines contributing to yeast allergy is theoretical.<sup>5</sup>

### Cell lines

Cell lines refer to a specific population of cells that are maintained in culture for extended periods. Cells used in cell lines can undergo spontaneous and unlimited replication, producing an unlimited lifespan for the cells, and a cell source that is continuously available. This removes the need for ongoing harvesting. More than 5000 human and animal cell lines are available. Those used in vaccine manufacture include two diploid cell strains of human origin (MRC-5 and WI-38), simian-derived continuous and diploid cell lines, chick embryo and chick embryo fibroblasts.<sup>14</sup> Residual proteins from these cell lines may be present to a varying degree in the vaccines produced from them. However,

vaccines undergo purification processes to remove cellular residuals and have maximum limits placed on their presence.<sup>14</sup>

### Concern regarding use of human cell lines

Certain cell lines (human diploid cell lines WI-38 and MRC-5) were derived from embryonic tissue from three elective, medically indicated abortions conducted in the 1960s.<sup>25</sup> This has raised concerns, with reports of some individuals with religious objections to abortion refusing vaccination because they feel this makes them complicit with the original act of abortion.<sup>26</sup>

Patients should be aware that cell lines are self-sustaining and are not the end therapeutic product; thus additional abortions are not needed to sustain vaccine manufacture.<sup>25,26</sup> No human cells are actually present in the vaccine, and no abortions are conducted specifically for the purpose of harvesting cell lines. Ethicists at the US National Catholic Bioethics Center have concluded that the association between certain vaccines and abortion was non-complicit, and thus use of these vaccines is not contrary to a religious opposition to abortion.<sup>27</sup>

### Religious and philosophical concerns regarding use of animal products

Some religious groups who have dietary restrictions for certain animal products may be concerned about their presence in vaccines. Ingestion of pork products is forbidden in Islam, and some Muslims may avoid medications that contain pork-derived products.<sup>28</sup> However, Shariah law includes the principle of “transformation”, where objects can be changed into another object with totally different properties and character, and this can turn unclean objects into clean and permissible objects. Within such a ruling, gelatin made from an unclean animal may be clean and permissible to ingest.<sup>29</sup>

Jews and Seventh-day Adventists also consider pork to be unclean. However, Jewish law permits use of porcine-derived products in non-edible forms such as parenteral formulations, or binding agents in tablets.<sup>30</sup> Similarly, pork-derived medical products are not prohibited for Seventh-day Adventists, although some individuals may prefer to avoid such products (Dr P Harrold, Associate Director of Adventist Health Ministries, South Pacific Division, personal communication, May 2005). Some strict vegetarians or vegans may also choose to avoid animal products in medications and vaccines; this is largely a personal choice and is likely to vary among individuals.

### Concern regarding risk of bovine spongiform encephalopathy (BSE)

Use of bovine-derived products in vaccine manufacture, such as gelatin or bovine sera, has prompted concern about whether this poses a risk of BSE. BSE is transmitted by prions, which may lead to Creutzfeldt-Jakob disease (vCJD) in humans.

A number of issues indicate that vaccination was not a contributing factor in the cases of vCJD in the United Kingdom. Most of these people would have been vaccinated before the emergence of BSE in British cattle.<sup>31</sup> Additionally, vaccines are used internationally, yet the outbreak of vCJD in humans was largely restricted to the UK. Gelatin is rated as a low-risk product. Bovine serum is not actually present in the final vaccine product, and the cells that contribute to the vaccine are not able to replicate prions.<sup>32</sup>

Despite administration of tens of millions of doses of vaccines manufactured using bovine-derived material, there are no reported cases of BSE transmission via human or animal vaccination. Because of these factors, the risk is considered theoretical.<sup>24,32-34</sup> Australian reviews have concluded that vaccines used in Australia meet high safety standards and that any risk of vaccines being contaminated with BSE is extremely low. Australian, European and US regulatory bodies have developed guidelines for use of bovine material in vaccine manufacture to minimise risk of BSE transmission.<sup>24,32-34</sup>

Bovine material must be sourced from countries where no recorded cases of BSE have occurred and an appropriate system of monitoring and reporting of BSE in animals has been implemented. Alternatively, bovine material may be sourced from specific donor herds where animal health is routinely monitored.

Use of manufacturing processes, such as heat sterilisation and chemical treatment, reduces or removes BSE infectivity from bovine products.

### Live vaccines

Non-living vaccines contain dead organisms or their components, which have been inactivated or killed by heat or chemical treatment.<sup>35</sup> In contrast, live attenuated vaccines contain live organisms that have lost the ability to cause serious disease, but retain sufficient antigenicity to cause an immune response that will protect against the original organism. These vaccines carry a risk of organisms reverting to virulent forms that cause infection rather than immunity, but this is rare. Oral polio vaccine, for example, has been reported to produce about one case of vaccine-associated paralytic poliomyelitis for every 2.4 million doses distributed.<sup>36</sup> Although not routinely used in Australia, the bacille Calmette-Guerin (BCG) vaccine may produce abscesses, regional lymphadenopathy and disseminated disease in immunocompromised patients.<sup>37</sup> Because of such risks, live vaccines are not recommended for routine use in pregnant or immunosuppressed patients.<sup>7</sup>

### Formaldehyde

Formaldehyde is used in the manufacture of killed vaccines to inactivate the pathogenic effects of the organism, while preserving antigenicity.<sup>5</sup> Concerns about the presence of formaldehyde are based on its toxicological profile and suggestions that it may act as a carcinogen. Although industrial exposure to formaldehyde may be associated with certain cancers, cancer risk has not been fully established and may relate to degree of exposure.<sup>38</sup> The current standard for Australian vaccines is a maximum of 0.02% w/v of free formaldehyde. During testing of Australian vaccines by the TGA, the maximum formaldehyde concentration detected was 0.004% w/v.<sup>7</sup>

### Latex

Patients may be exposed to latex during vaccination via its presence in syringe plungers and vial stoppers. Latex contains numerous polypeptides, many of which may act as allergens; case reports describe various immediate-type hypersensitivity reactions occurring post-vaccination in patients with a history of latex allergy, including anaphylaxis.<sup>39</sup> Removal of rubber stoppers or use of alternative delivery techniques are options for patients with a history of serious latex allergy.

### Conclusions

Every decision to undertake medical interventions involves a risk-benefit assessment. Vaccination decisions are made more emotive because of the influence of the anti-vaccination lobby. Patients' concerns about vaccine components need to be taken seriously. However, accessing accurate information about vaccine constituents, components and their safety is difficult for the busy health professional. We have sought to fill this gap. Provision of accurate, substantiated and unemotional information enables both health professionals and the public to make informed decisions concerning vaccination risk.

### Competing interests

None identified.

### References

- World Health Organization. Vaccines, immunization and biologicals: diseases and vaccines. The history of vaccination. Available at: <http://www.who.int/vaccines-diseases/history/history.shtml> (accessed Dec 2005).
- Australian Bureau of Statistics. Occasional paper: vaccination coverage in Australian children — ABS statistics and the Australian Childhood Immunisation Register (ACIR). Canberra: ABS, 2003. (ABS Catalogue No. 4813.0.55.001.)
- Gilbert GL, Gidding HF, Backhouse J, McIntyre PB. Varicella seroprevalence and vaccine uptake in preschool children [letter]. *Med J Aust* 2005; 182: 42.
- Begg N, Ramsay M, White J, Bozoky Z. Media dents confidence in MMR vaccine. *BMJ* 1998; 316: 561.
- Offit PA, Jew RK. Addressing parents' concerns: do vaccines contain harmful preservatives, adjuvants, additives, or residuals? *Pediatrics* 2003; 112: 1394-1397.
- Pichichero ME, Cernichiari E, Lopreiato J, Treanor J. Mercury concentrations and metabolism in infants receiving vaccines containing thiomersal: a descriptive study. *Lancet* 2002; 360: 1737-1741.
- National Health and Medical Research Council. The Australian Immunisation Handbook. 8th ed. Canberra: NHMRC, 2003. Available at: <http://immunise.health.gov.au/handbook.htm> (accessed Dec 2005).
- Wakefield AJ, Murch SH, Anthony A, et al. Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children. *Lancet* 1998; 351: 637-641.
- Murch SH, Anthony A, Casson DH, et al. Retraction of an interpretation. *Lancet* 2004; 363: 750.
- Parker SK, Schwartz B, Todd J, Pickering LK. Thimerosal-containing vaccines and autistic spectrum disorder: a critical review of published original data. *Pediatrics* 2004; 114: 793-804.
- Patrizi A, Rizzoli L, Vincenzi C, et al. Sensitization to thimerosal in atopic children. *Contact Dermatitis* 1999; 40: 94-97.
- Vogt T, Landthaler M, Stolz W. Generalized eczema in an 18-month-old boy due to phenoxyethanol in DPT vaccine. *Contact Dermatitis* 1998; 38: 50-51.
- Georgitis JW, Fasano MB. Allergenic components of vaccines and avoidance of vaccination-related adverse events. *Curr Allergy Rep* 2001; 1: 11-17.
- Finn TM, Egan W. Vaccine additives and manufacturing residuals in the United States — licensed vaccines. In: Plotkin SA, Orenstein WA, editors. *Vaccines*. 4th ed. Philadelphia: WB Saunders, 2004.
- HogenEsch H. Mechanisms of stimulation of the immune response by aluminum adjuvants. *Vaccine* 2002; 20 Suppl 3: S34-S39.
- Agency for Toxic Substances and Disease Registry. Toxicological profile for aluminium. Atlanta: US Department of Health and Human Services, Public Health Service, 1999. Available at: <http://www.atsdr.cdc.gov/tox-profiles/tp22.html> (accessed Dec 2005).
- Kaaber K, Nielsen AO, Veien NK. Vaccination granulomas and aluminium allergy: course and prognostic factors. *Contact Dermatitis* 1992; 26: 304-306.
- Fawcett HA, Smith NP. Injection-site granuloma due to aluminum. *Arch Dermatol* 1984; 120: 1318-1322.

- 19 Jefferson T, Rudin M, Di Pietrantonj C. Adverse events after immunisation with aluminium-containing DTP vaccines: systematic review of the evidence. *Lancet Infect Dis* 2004; 4: 84-90.
- 20 Brenner A. Macrophagic myofasciitis: a summary of Dr. Gherardi's presentations. *Vaccine* 2002; 20 Suppl 3: S5-S6.
- 21 Rottem M, Shoenfeld Y. Vaccination and allergy. *Curr Opin Otolaryngol Head Neck Surg* 2004; 12: 223-231.
- 22 James JM, Zeiger RS, Lester MR, et al. Safe administration of influenza vaccine to patients with egg allergy. *J Pediatr* 1998; 133: 624-628.
- 23 Andrews RM, Kempe AE, Sinn KK, Herceg A. Vaccinating children with a history of serious reactions after vaccination or of egg allergy. *Med J Aust* 1998; 168: 491-494.
- 24 Castle P, Robertson JS. Summary and conclusion. In: Brown F, Cartwright T, Horaud F, Spieser JM, editors. *Animal sera, animal sera derivatives and substitutes used in the manufacture of pharmaceuticals: viral safety and regulatory aspects*. Basel: Karger, 1999.
- 25 Grabenstein JD. Where medicine and religion intersect. *Ann Pharmacother* 2003; 37: 1338-1339.
- 26 Rudd G. Is vaccination complicit with abortion? *Ann Pharmacother* 2003; 37: 1340-1341.
- 27 Maher DP. Vaccines, abortion and moral coherence. *Natl Cathol Bioeth Q* 2002; 2: 51-67.
- 28 Bashir A, Asif M, Lacey FM, et al. Concordance in Muslim patients in primary care. *Int J Pharmacy Pract* 2001; 9(Suppl): R78.
- 29 Islamic Organization for Medical Sciences. The use of unlawful or juridically unclean substances in food and medicine. Question 104. Islam SET [website]. Available at: <http://www.islamset.com/qa/index.html> (accessed Dec 2005).
- 30 Mynors G, Ghalamkari H, Beaumont S, et al. Informed choice in medicine taking. Drugs derived from pigs and their clinical alternatives: an introductory guide. London: Medicines Partnership, 2004. Available at: <http://www.medicines-partnership.org/our-publications/drugs-of-porcine-origin> (accessed Dec 2005).
- 31 Minor PD, Will RG, Salisbury D. Vaccines and variant CJD. *Vaccine* 2000; 19: 409-410.
- 32 European Agency for the Evaluation of Medicinal Products. Questions and answers on bovine spongiform encephalopathies (BSE) and vaccines. London: European Medicines Agency, 2001. Available at: <http://www.emea.eu.int/pdfs/human/bwp/081901en.pdf> (accessed Dec 2005).
- 33 US Food and Drug Administration. Center for Biologics Evaluation and Research. Questions and answers on bovine derived materials used in vaccine manufacturing. Available at: <http://www.fda.gov/cber/bse/bseqa.htm#a3> (accessed Mar 2005).
- 34 Therapeutic Goods Administration. Questions and answers on BSE risk associated with the use of materials of bovine origin during the manufacture of vaccines. Available at: <http://www.tga.gov.au/docs/html/bse-faq.htm> (accessed Mar 2005).
- 35 Egbert GB, Mascolo ED, Egan W. Vaccine manufacturing. In: Plotkin SA, Orenstein WA, editors. *Vaccines*. Philadelphia: WB Saunders; 2004.
- 36 Burgess MA, McIntyre PB. Vaccine-associated paralytic poliomyelitis. *Commun Dis Intell* 1999; 23: 80-81.
- 37 Talbot EA, Perkins MD, Silva SF, Frothingham R. Disseminated bacille Calmette-Guerin disease after vaccination: case report and review. *Clin Infect Dis* 1997; 24: 1139-1146.
- 38 Hauptmann M, Lubin JH, Stewart PA, et al. Mortality from solid cancers among workers in formaldehyde industries. *Am J Epidemiol* 2004; 159: 1117-1130.
- 39 Russell M, Pool V, Kelso JM, Tomazic-Jezic VJ. Vaccination of persons allergic to latex: a review of safety data in the Vaccine Adverse Event Reporting System (VAERS). *Vaccine* 2004; 23: 664-667.

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## John Glenton Watson

BA, BEc, MBBS, FRACGP, FRACMA

A LOVED AND RESPECTED GENERAL PRACTITIONER in Sydney's Eastern Suburbs for many years, John Watson came from humble beginnings. Excelling in many intellectual pursuits, he was an eternal student. He loved teaching, and always had a close association with the University of Sydney and Sydney Hospital.

John was born in Sydney on 26 May 1917. He always wanted to be a doctor, but during the Depression no child of a poor family could afford the fees. He won a Teachers' College scholarship and became a science teacher. While teaching by day, he attended evening classes in economics at the University of Sydney.

After serving in the Australian Military Forces from 1941 to 1946, John returned to teaching. At the same time, he completed Bachelor of Arts and Bachelor of Economics degrees as an evening student, while saving to enrol in medicine. In 1948, he began to study medicine at the University of Sydney, supplementing his income by working as a bookmaker's clerk. His sharpness as a mathematician was valued, although his knowledge of and interest in racing was nil! In 1950, he married Rose Wicks, also a teacher, who helped to support him through medical school.

After graduation in 1954, John was appointed Junior Resident at Sydney Hospital. In 1956, approaching the age of 40, he established a 24-hours-a-day, 7-days-a-week general practice in South Coogee, living on the premises. Many of his patients became lifelong friends.

When Medicare was introduced, John felt he could not work under a system that "put the clock" on time spent with a patient, so he went into hospital administration, becoming Deputy Superintendent at Sydney Hospital. Although a capable administrator, he found some aspects of the work very tedious and missed the contact with patients, and so eventually returned to limited general



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practice in South Coogee. He served many years as an Honorary Medical Officer in the Sydney Hospital general medicine and neurology outpatient clinics.

John's love of learning, teaching and patient care continued all his life. He was one of the first "radio talk-back doctors" to answer listeners' questions over the air. For many years he was a member of the Editorial Board of *The Medical Journal of Australia*. He taught medicine and medical principles at the School of Occupational Therapy, and later became a director of the Sydney Medical Emergency Service Co-op, which provided an out-of-hours locum service to GPs. He was also in great demand as an after-dinner speaker and as a lecturer for the University of the Third Age.

His other interests, as a student and beyond, included debating (the University of Sydney's JG Watson trophy for debating was named after him) and compering and scriptwriting for the annual Sydney University revue. He was President of the Sydney University Union and later a student representative Fellow of the University Senate. He had a keen interest in many sports, including surfing, fishing, cricket, rugby, athletics and hockey. At an advanced age, he took up piano playing and landscape painting.

John died on 6 July 2005 after several cerebral vascular incidents and eventual multiple organ failure. He was a truly good man, who touched many people in his different roles. He will be sadly missed by Rose, his sons John, Ian and Andrew, and their families and many friends.

Frederick O Stephens