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Cochrane Database of Systematic Reviews 1998, Issue 1. Art. No.: CD000975.

DOI: 10.1002/14651858.CD000975.pub2.

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Vaccines for preventing anthrax

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Editorial group: Cochrane Infectious Diseases Group.

Publication status and date: Unchanged, published in Issue 5, 2019.

Citation: Jefferson T, Demicheli V, Deeks JJ, Graves PM, Pratt M, Rivetti D. Vaccines for preventing anthrax. *Cochrane Database of Systematic Reviews* 1998, Issue 1. Art. No.: CD000975. DOI: 10.1002/14651858.CD000975.pub2.

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ABSTRACT

Background

Anthrax is a potentially fatal bacterial disease with cutaneous, inhalation, and gastrointestinal forms. Three anthrax vaccines are commercially available, but their comparative effectiveness and safety is not clear.

Objectives

To assess the effectiveness and safety of vaccines against human anthrax in relation to adverse effects and disease incidence.

Search methods

We searched the Cochrane Infectious Diseases Group Specialized Register (March 2004), CENTRAL (*The Cochrane Library* Issue 3, 2005), MEDLINE (1966 to September 2005), EMBASE (1988 to September 2005), Science Citation Index (1981 to September 2005), the U.S. National Institutes of Health (NIH; September 2005), and the reference lists of articles. We contacted the UK Ministry of Defence, US Department of Defense, and individual researchers in the field.

Selection criteria

Prospective randomized, quasi-randomized, and cluster randomized controlled trials comparing anthrax vaccines with placebo, other (non-anthrax) vaccines, or no intervention.

Data collection and analysis

Six reviewers independently assessed trial methodological quality and extracted data. Adverse effects data was collected from the trials.

Main results

Two trials involving 16,052 people met the inclusion criteria. Both trials had methodological limitations. Compared to placebo, vaccination was associated with a reduced risk of contracting anthrax (Relative Risk 0.16; 95% confidence interval 0.07 to 0.35). In the one trial reporting adverse effects, the killed vaccine was associated with a higher incidence of adverse effects compared to the placebo (Peto odds ratio 5.15; 95% confidence interval 2.28 to 11.61). Just over 5% of participants in the vaccine group reported adverse effects. The effectiveness of the vaccine does not appear to be influenced by the route of inoculation (scarification compared to needless injection - odds ratio 1.61; 95% confidence interval 0.39 to 6.75).

Authors' conclusions

Killed anthrax vaccines appear to be effective in reducing the risk of contracting anthrax with low rate of adverse effects. Further research should be carried out on the short and long term safety effects of available vaccines and if possible their effectiveness.

PLAIN LANGUAGE SUMMARY

Vaccines for preventing anthrax

Plain language summary pending

BACKGROUND

Anthrax is an acute bacterial disease derived from animals caused by *Bacillus anthracis*. The portal of entry is either through skin abrasions, inhalation, or ingestion. Three forms of the disease are thus possible: cutaneous (the most common), respiratory, and gastrointestinal. The cutaneous form starts as a painful skin ulcer which heals leaving a coal-black plug (eschar) which gives its Greek name to the disease (anthrax is the word for coal). In approximately 10 percent of cases, cutaneous anthrax can progress to systemic disease in people who are not treated with antibiotics (Dixon 1999).

The respiratory form resembles at the beginning an upper respiratory tract infection and quickly develops into septicaemia and toxic shock. The gastrointestinal form usually manifests itself with violent abdominal pain and bloody diarrhoea. Death in all forms is usually from septicaemia (blood infection) and more rarely meningitis (infection of the membrane over the brain). The respiratory and gastrointestinal forms of the disease have a very high fatality rate (Dixon 1999).

Anthrax is a disease of herbivorous animals that ingest or inhale *B. anthracis* spores while feeding. When terminally ill, such animals shed bacilli with blood and body fluids (Dixon 1999). The bacilli produce hardy spores (survival form of the agent which can remain active for long periods of time) when exposed to the outside environment. Humans mainly contract the cutaneous disease when exposed to hides of animals or other materials containing spores, breathe air heavily contaminated by spores, or eat contaminated foodstuffs.

Anthrax is mainly a disease of agricultural workers and an occupational hazard of tanners. Anthrax is found throughout the world but concentrated in Europe, Africa, and Asia (Dixon 1999). The pathogenicity (capacity to cause disease) of the bacilli is dependent on production of three antigens: protective antigen (PA), lethal

factor (LF), and edema factor (EF). The three components combine to form two potent toxins: oedema toxin and lethal toxin. Interventions against anthrax range from prevention through education of operators and dust control, to treatment with penicillin, disinfection, and isolation of suspected cases.

Human vaccines against the bacillus were developed in the 1950s and 60s. At present three vaccines are commercially available: the Georgian/Russian, the UK, and the USA vaccines. These vaccines are thought to work through their capacity to stimulate immunity to PA, LF, and EF. PA is thought to confer protection, making it a good candidate for a vaccine. However, PA on its own is not thought to be enough to stimulate cell mediated immunity, and other antigens are necessary (Dixon 1999). Anthrax vaccines can be administered via the aerosol or cutaneous (skin) route. The latter can be done by removing a fragment of the upper layer of the skin (scarification) to allow the absorption of the vaccine.

The Georgian/Russian vaccines are produced by the Tblisi Research Institute of Vaccines and Serums located in the former USSR Republic of Georgia. They consist of live spores from a Stern strain of *B. anthracis*, and the vaccine is administered in the shoulder by scarification. Apparently other sites in the former USSR are also involved in the production of similar vaccines (Dr Tim Brooks, personal communication).

The UK and USA vaccines consist of alum-precipitated cell-free filtrate of bacilli (sometimes called supernatant particles). The USA vaccine, manufactured by the Michigan Department of Public Health, is adsorbed onto aluminium-hydroxide (so called adsorbed anthrax vaccine, or AVA). It is thought that both vaccines have low LF and EF content, but high PA content.

In the UK, vaccination is recommended only for workers at risk of exposure to anthrax (personnel of tanneries processing wool or hides and bone). More recently vaccination of military personnel and key workers has been undertaken on a compulsory (as in the

USA) or voluntary basis (as in the UK). The vaccine is administered with four injections of 0.5 ml with intervals of three weeks between the first three injections and six months between the third and fourth. A booster dose should be given yearly (Salisbury 1996).

Although the first recorded immunization against anthrax in animals dates back to 1880 (Turnbull 1991), until recently there has been little research into anthrax vaccines other than that carried out for antibacteriological warfare purposes by the military. Yet this has resulted in casualties during peace time: between April and May 1979 there was an outbreak of anthrax in the area immediately downwind of a military microbiological facility at Sverdlovsk in Russia (Meselson 1994). Ninety six cases of anthrax were reported; of these 64 died (Meselson 1994). This outbreak was probably due to accidental release of spores into the air from the military laboratories connected with the use of *B. anthracis* for biological warfare. Adverse effects are important, as soldiers are sometimes immunised with the vaccine: for example, in 1990-91 British troops deployed during the Gulf War were immunised with the UK vaccine as a precaution against possible use of *B. anthracis* as an airborne weapon by the Iraqis. More recently there has been a resurgence of interest in the use of anthrax as a biological weapon after the attacks to the USA and the terrorist anthrax postal campaign.

In the search for new vaccines, manufacturers have aimed for better quality purified PA vaccines with better adjuvants; vaccines made through recombinant gene technology (*B. subtilis*, baculovirus, or *Vaccinia* virus expressing the PA gene); and mutant vaccines with altered PA, EF, and LF sequences to render them avirulent but immunogenic (Dixon 1999).

Despite these developments, several issues are unresolved, including the comparative effectiveness and safety of existing vaccines.

OBJECTIVES

To assess the effectiveness and safety of vaccines against human anthrax in relation to adverse effects and disease incidence.

METHODS

Criteria for considering studies for this review

Types of studies

Prospective randomized and quasi-randomized controlled trials. Cluster randomized controlled trials.

Types of participants

Well adults or children irrespective of immune status or special risk category.

Types of interventions

Intervention: Live attenuated (capable of reproduction but not of causing the disease) or killed (neither capable of reproduction or of causing the disease) vaccines administered by any route.

Control: Placebo; other (non-anthrax) vaccines; or no intervention.

Types of outcome measures

PRIMARY

Numbers of cases avoided by vaccination (number of cases divided by the number vaccinated/not vaccinated in the defined geographical study area).

A case was defined clinically.

ADVERSE EFFECTS

Local and systemic adverse effects.

Systemic adverse effects included malaise, nausea, fever, arthralgias, rash, headache, and more generalized and serious signs.

Local adverse effects were defined as including local oedema at the site of inoculation.

Search methods for identification of studies

We attempted to identify all relevant studies regardless of language or publication status (published, unpublished, in press, and in progress).

We searched the Cochrane Infectious Diseases Group specialized trials register for relevant trials up to September 2005 using the search terms: anthrax; and bacillus anthracis. Full details of the Cochrane Infectious Diseases Group methods and the journals hand searched are published in The Cochrane Library in the section on Collaborative Review Groups.

We searched the Cochrane Central Register of Controlled Trials (CENTRAL), published in *The Cochrane Library* (Issue 3, 2005) using the search terms: anthrax; and bacillus anthracis. This contains mainly reference information to randomized controlled trials and controlled clinical trials in health care.

We also searched the following electronic databases using the topic search terms in combination with the search strategy for retrieving trials developed by the Cochrane Collaboration and detailed in the Cochrane Reviewers' Handbook (Clarke 2000):

(1) MEDLINE (1966 to September 2005) using the search terms: anthrax; anthrax vaccines; bacillus anthracis; anthrax vaccine adsorbed; and AVA.

(2) EMBASE (1988 to September 2005) using the search terms: anthrax; anthrax vaccine; anthrax toxin; bacillus anthracis; anthrax vaccine adsorbed; and AVA.

(3) Science Citation Index (1981 to September 2005) using the search terms: anthrax; bacillus anthracis; bacillus-anthraxis; and AVA.

(4) U.S. National Institutes of Health (NIH; <http://clinicaltrials.gov/>; accessed 7 September 2005) using the search term: anthrax.

We contacted the UK Ministry of Defence, US Department of Defense, individual researchers, and former intelligence officers working in the field for unpublished data and confidential reports. We also checked the reference lists of all trials identified by the above methods.

Data collection and analysis

STUDY SELECTION

Tom Jefferson scanned the results of the literature search for potentially relevant trials. TJ retrieved the full papers for all potentially relevant trials.

ASSESSMENT OF METHODOLOGICAL QUALITY

Tom Jefferson, V Demicheli, and Jon Deeks independently assessed the potentially relevant trials for inclusion in the review. Six reviewers independently checked this assessment and there were no disagreements.

We used the following criteria to assess the methodological quality of each trial: method of randomization; allocation concealment; blinding; and effects of withdrawals. We classified blinding methods as adequate if neither the person doing the assessment nor the study participant could identify the intervention being assessed (double blind), or if in the absence of such a statement, the authors mention the use of active placebo, identical placebo, or dummies.

DATA EXTRACTION

Three reviewers independently extracted data.

DATA ANALYSIS

We calculated disease rates as the ratio of the number of cases to the number of participants included in each group, which ignores any between trial variation in effectiveness related to different lengths of follow up. As cases were very rare, the Relative Risk was very similar to the odds ratio, which was used to combine the study results.

We visually examined the forest plot for heterogeneity. Although the [Burgasov 1976](#) trial was cluster randomized, it has not been possible to make an appropriate adjustment in this analysis due to lack of information in the original trial. The impact of ignoring cluster randomization depends on the independence of the anthrax cases within the study. If some of the cases did occur within the same villages the precision of the treatment effect is overestimated, but given the very low disease rates it seems unlikely that this would substantially change the conclusions.

We stratified our meta-analysis by type of vaccine used (live attenuated or killed), severity of adverse effects (local or systemic), and means of administration (scarification or needle-less). The latter method involves the use of a high pressure device which squirts vaccine through a small skin wound caused by the jet.

RESULTS

Description of studies

We identified three potentially relevant trials ([Derbin 1981](#), [Brachman 1962](#), [Burgasov 1976](#)), of which two met the inclusion criteria ([Brachman 1962](#), [Burgasov 1976](#)).

[Brachman 1962](#) assessed the effectiveness of the protective antigen USA vaccine to protect against cutaneous and inhalation of anthrax in 1249 adult workers in 4 goat hair processing mills in the North East of the USA in the 1950s. Controls were given 0.1 percent alum placebo. The incidence of anthrax was 1.2 per 100 person years. The follow up in the 4 mills varied from 6 to 28 months, the overall average being 16 months. The outcomes considered were cases of anthrax, incidence and severity of adverse effects.

[Burgasov 1976](#), translated from a summary document in Russian, is a large random cluster intervention study of anthrax vaccine comparing no vaccine. It used three comparison groups: inoculation by needleless injector, by scarification, and a control arm. 157,259 people in 228 locations in the Kazakh Soviet Socialist Republic (now the Republic of Kazakhstan) took part in the early 1970s. The incidence of anthrax in Kazakh was 0.0154 cases per 100 person years. The vaccine is thought to be a Stern strain variant (STI) consisting of live, attenuated organisms, without their bacterial capsule. The follow up was for two years and the outcome considered was cases of anthrax.

Risk of bias in included studies

Both trials failed to report clear allocation concealment procedures and reported taking inadequate measures to protect double blinding. However, [Brachman 1962](#) had adequate measures to deal with withdrawals from the study and [Burgasov 1976](#) reported an adequate system of random cluster sampling and stratification by baseline risk in the 228 localities in which the trial had taken place.

Although [Brachman 1962](#) did not mention randomization in the text, they administered placebo to the control arm in a single blind fashion. [Burgasov 1976](#) described the randomization process, but made no mention of blinding or how they took withdrawals from the trial into account.

Effects of interventions

Estimates of overall effectiveness and safety favour vaccination, the Peto odds ratio for cases of anthrax being 0.18 (95% confidence interval 0.10 to 0.34). The corresponding Relative Risk (RR) of anthrax is 0.16 (95% confidence interval 0.07 to 0.35), and from this we can estimate vaccine efficacy in terms of cases of anthrax avoided, as $1 - \text{RR} = 0.84$ (95% confidence interval 0.65 to 0.93) or 84% (65 to 93%). The Chi-square test for heterogeneity of the two studies included in the meta analysis showed no statistically significant difference between the results of the two trials.

The potential impact of the vaccination varies between setting. In the high incidence setting of Brachman mills (1.2 cases per 100 person years), vaccination of 99 people will prevent 1 case of anthrax per year. In the lower incidence setting of the Kazakh trial (0.0154 cases per 100 person years), vaccination of 7730 people is needed to prevent one additional case of anthrax.

Brachman 1962 showed that the killed vaccine was found to be 92.5% effective in preventing cases of anthrax. Separate effectiveness estimates for cutaneous and inhalation forms are not given but the small numbers of inhalation anthrax found in their study led them to be unable to conclude protective benefit. Local prominent reactions, typically erythema (redness), induration (thickening), and oedema (swelling), at the site of inoculation occurred in 5.5% of cases and lasted 24 to 48 hours while systemic reactions occurred in 0.5% of cases with local oedema and malaise (generalized aches and pains) of 24 hours duration. Two of three vaccinees who had natural immunity to anthrax experienced severe local reactions lasting up to 48 hours with arm swelling and malaise. There were statistically significant more participants with an adverse effect in the group receiving the killed vaccine compared to the control alum-based placebo (Peto odds ratio 5.15; 95% confidence interval 2.28 to 11.61) (Brachman 1962).

Burgasov 1976 reported that the Stern strain variant vaccine afforded 75.0% protection when administered by scarification and 84.2% when administered by the needleless gun method. This difference in outcome was hypothesized to occur because of non-standard application of scarification, but was not statistically significant (odds ratio 1.61; 95% confidence interval 0.39 to 6.75). No adverse effect data are reported.

DISCUSSION

The results of our review show that there are several limits to the knowledge of the effects of anthrax vaccines. There appear to be few comparative studies and those which are available assess the older generation of vaccines and show several methodological

weaknesses. These are: uncertain case definitions; unclear vaccination schedules; and weak experimental design. We assessed and excluded non-comparative studies reporting safety surveillance data. Despite such weaknesses and the fact that the two studies in this review assess two different types of vaccines (killed and attenuated), we believe that the data presented in this review show that overall anthrax vaccines are safe and efficacious. Most of the evidence depends on the study by Burgasov 1976, which was a large, relatively well designed study carried out in a relatively high incidence former Soviet Socialist Republic, now called the Republic of Kazakhstan. In this study a live attenuated vaccine was used which is different than the current fractionated supernatant vaccines in service in the UK and USA. Given the use of anthrax vaccine adsorbed (AVA) in the USA and the UK vaccine in the military and their possible future use to protect key workers from bacteriological warfare threats, we believe that a large, well designed randomized controlled trial of current vaccines to assess short and long term safety effects and, if possible, effectiveness should be carried out. We are disappointed at our inability to identify trials of the newer vaccine formulations, but have no reason to believe that such trials exist.

AUTHORS' CONCLUSIONS

Implications for practice

Anthrax vaccine should be administered to persons exposed at high risk of the disease. The incidence and severity of adverse effects, although perhaps variable from batch to batch, is low. No comment can be made on the comparison of effectiveness of the two vaccines as no study has compared them directly.

Implications for research

Although old killed vaccines appear effective and relatively well tolerated there are insufficient comparative data on short and long term safety of current vaccines.

A large, well designed randomized controlled trial to assess these should be carried out.

ACKNOWLEDGEMENTS

R Behrens, F Bottasso, A MacMillan A, and C Morris helped assess trial quality.

The reviewers would like to thank Dr Tim Brooks, Mrs Carol Hobbs, and Mrs Judy Dance for providing help.

REFERENCES

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Brachman 1962 *{published data only}*

Brachman PS, Gold H, Plotkin SA, Fekety FR, Werrin M, Ingraham NR. Field evaluation of a human anthrax vaccine. *American Journal of Public Health* 1962;**52**:632–45.

Burgasov 1976 *{published data only}*

Burgasov PN, Cherkasskij BL, Knop AG, Utengov KU. Epidemiological efficacy of the anthrax STI vaccine [in Russian]. Moscow: Scientific Research Institute of Epidemiology, 1976.

References to studies excluded from this review

Derbin 1981 *{published data only}*

Derbin MI, Sadovoj NV, Tarumov VS, Garin NS. A comparative study of humoral anti-anthrax immunity in animals and humans immunised with live and chemical vaccines [in Russian]. Moscow: Central Scientific Research Institute of Epidemiology, 1981.

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Pittman 2002 *{published data only}*

Pittman PR, Kim-Ahn G, Pifat DY, Coonan K, Gibbs P, Little S, et al. Anthrax vaccine: immunogenicity and safety of a dose-reduction, route-change comparison study in humans. *Vaccine* 2002;**20**(9-10):1412–20.

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Salisbury 1996

Salisbury DM, Begg NT editors. Immunisation against infectious disease. Edward Jenner Bicentary. London: HMSO, 1996:61–2.

Turnbull 1991

Turnbull PCB. Anthrax vaccines: past, present and future. *Vaccine* 1991;**9**:533–9.

* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Brachman 1962

Methods	Single blinded placebo controlled study.	
Participants	1249 adult workers in 4 tanneries in the North East of the USA in the 1950s 379 workers were vaccinated, 414 were assigned to placebo. Additionally 116 workers did not complete the vaccination cycle and 340 refused to take part in the study	
Interventions	Protective antigen (R1-NP strain) vaccine made from sterile culture filtrate produced by the US Army 0.5 ml was administered subcutaneously in 3 doses at weeks 0, 2, and 4 The primary cycle was followed by 3 booster doses (0.5ml) at 6-monthly intervals Placebo contained a solution of 0.1% alum. Although the study was carried out between 1955 and 1959, the average length of exposure was 16 months, given the rolling nature of the immunization programme The follow up in the 4 mills varied from 6 to 28 months, the overall average being 16 months	
Outcomes	Cases of anthrax. Incidence and severity of adverse effects (divided into local and systemic) A “clinical” case definition was used (ie, with no laboratory confirmation)	
Notes	The incidence of anthrax was 1,200 per 100,000/year in the 4 tanneries Overall the vaccine was found to be 92.5% effective in preventing cases of anthrax	
<i>Risk of bias</i>		
Bias	Authors’ judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Burgasov 1976

Methods	Random cluster intervention study of anthrax vaccine compared to placebo in 3 arms	
Participants	157,259 people in the Kazakh Soviet Socialist Republic spread in 228 sites in which anthrax was endemic 52,763 people were assigned to the needleless injection group 54,522 were assigned to the scarification group. 49,974 were assigned to the control (no intervention) group.	
Interventions	Stern strain variant (STI) vaccine consisting of live, attenuated organisms, without their bacterial capsule administered either by needleless gun or by scarification compared to no vaccination No schedule is given. Participants were followed up for 2 years.	

Burgasov 1976 (Continued)

Outcomes	Anthrax cases. Case definition was “bacteriological”.	
Notes	The study was undertaken in the Kazakh Soviet Socialist Republic, now the Republic of Kazakhstan The annual incidence of anthrax in the Republic was 15.4 cases per 100,000/year	
<i>Risk of bias</i>		
Bias	Authors’ judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Derbin 1981	Nonrandomized, non-comparative study.

DATA AND ANALYSES

Comparison 1. Any vaccine compared with placebo/control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Cases of anthrax	2	158052	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.18 [0.10, 0.34]
1.1 Killed vaccine	1	793	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.18 [0.07, 0.49]
1.2 Attenuated vaccine	1	157259	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.18 [0.08, 0.41]

Comparison 2. Killed vaccine compared to placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2 Adverse effects	1		Peto Odds Ratio (Peto, Fixed, 95% CI)	Subtotals only
2.1 Local	1	793	Peto Odds Ratio (Peto, Fixed, 95% CI)	5.15 [2.28, 11.61]
2.2 Systemic	1	793	Peto Odds Ratio (Peto, Fixed, 95% CI)	8.13 [0.51, 130.48]
2.3 Any adverse effects	1	793	Peto Odds Ratio (Peto, Fixed, 95% CI)	5.15 [2.28, 11.61]

Comparison 3. Attenuated vaccine

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Cases of anthrax	1		Peto Odds Ratio (Peto, Fixed, 95% CI)	Subtotals only
1.1 Scarification administration	1	104496	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.30 [0.13, 0.67]
1.2 Needleless administration	1	102737	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.23 [0.10, 0.53]

Comparison 4. Attenuated vaccine - scarification vs needleless

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Cases of anthrax	1	107285	Odds Ratio (M-H, Fixed, 95% CI)	1.61 [0.39, 6.75]

Analysis 1.1. Comparison 1 Any vaccine compared with placebo/control, Outcome 1 Cases of anthrax.

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Comparison: 1 Any vaccine compared with placebo/control

Outcome: 1 Cases of anthrax

Analysis 2.2. Comparison 2 Killed vaccine compared to placebo, Outcome 2 Adverse effects.

Review: Vaccines for preventing anthrax

Comparison: 2 Killed vaccine compared to placebo

Outcome: 2 Adverse effects

Analysis 3.1. Comparison 3 Attenuated vaccine, Outcome 1 Cases of anthrax.

Review: Vaccines for preventing anthrax

Comparison: 3 Attenuated vaccine

Outcome: 1 Cases of anthrax

Analysis 4.1. Comparison 4 Attenuated vaccine - scarification vs needleless, Outcome 1 Cases of anthrax.

Review: Vaccines for preventing anthrax

Comparison: 4 Attenuated vaccine - scarification vs needleless

Outcome: 1 Cases of anthrax

WHAT'S NEW

Date	Event	Description
9 November 2008	Amended	Converted to new review format.

HISTORY

Protocol first published: Issue 2, 1997

Review first published: Issue 1, 1998

Date	Event	Description
15 November 2006	Amended	Review withdrawn as of Issue 1, 2007.
7 September 2005	New search has been performed	New studies sought but none found.
8 May 2002	Amended	Background, Description of studies and Characteristics of included studies revised. New search; and studies awaiting assessment
24 November 1997	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

All reviewers contributed to writing the protocol, screening the searches, data extraction and writing the final report. Jon J Deeks undertook data analysis.

DECLARATIONS OF INTEREST

We certify that we have no affiliations with or involvement in any organization or entity with a direct financial interest in the subject matter of the review (eg, employment, consultancy, stock ownership, honoraria, expert testimony).

SOURCES OF SUPPORT

Internal sources

- Ministry of Defence, UK.

External sources

- Department for International Development, UK.

NOTES

The Editor withdrew this review as of Issue 1, 2007. The review has been replaced. The citation for the new review is:

Donegan S, Bellamy R, Gamble CL. Vaccines for preventing anthrax. *Cochrane Database of Systematic Reviews* 2009, Issue 2. Art. No.: CD006403. DOI: 10.1002/14651858.CD006403.pub2.

INDEX TERMS

Medical Subject Headings (MeSH)

Anthrax [immunology; *prevention & control]; Vaccines [*therapeutic use]

MeSH check words

Adult; Humans