

PNEUMOVAX®

(Pneumococcal Vaccine, Polyvalent) MSD

INDICATIONS: PNEUMOVAX is indicated for immunization against lobar pneumonia and bacteremia, caused by those types of pneumococci included in the vaccine, in all persons two years of age or older in whom there is an increased risk of morbidity and mortality from pneumococcal pneumonia. These include: (1) persons having chronic physical conditions such as chronic heart disease of any etiology, chronic bronchopulmonary diseases, chronic renal failure, and diabetes mellitus or other chronic metabolic disorders; (2) persons in chronic care facilities; (3) persons convalescing from severe disease; (4) persons 50 years of age or older.

When PNEUMOVAX and FLUAX® (Influenza Virus Vaccine, MSD) were given simultaneously in separate extremities, antibody response and adverse effects were comparable to those which followed administration of the vaccines at different times. Before administering, see full prescribing information for FLUAX.

NOTE: Re-vaccination with PNEUMOVAX should not be carried out at intervals of less than three years.

CONTRAINDICATIONS: Hypersensitivity to any component of the vaccine. Epinephrine injection (1:1000) must be immediately available should an acute anaphylactoid reaction occur due to any component of the vaccine.

Do not give PNEUMOVAX to pregnant females; the possible effects of the vaccine on fetal development are unknown.

Children less than two years of age do not respond satisfactorily to the capsular types of PNEUMOVAX that are most often the cause of pneumococcal disease in this age group. Accordingly, PNEUMOVAX is not recommended in this age group.

PNEUMOVAX is not recommended for patients who have received extensive chemotherapy and/or nodal irradiation for Hodgkin's disease.

WARNINGS: PNEUMOVAX will not immunize against capsular types of pneumococcus other than those contained in the vaccine (see table below).

14 Pneumococcal Capsular Types Included in PNEUMOVAX													
Nomenclature							Pneumococcal Types						
US	1	2	3	4	6	9	12	14	19	23	35	51	56
Danish	1	2	3	4	6A	9	12F	14	19F	23F	35	7F	18C

If the vaccine is used in persons receiving immunosuppressive therapy, the expected serum antibody response may not be obtained. Intradermal administration may cause severe local reactions.

In patients who require penicillin (or other antibiotic) prophylaxis against pneumococcal infection, such prophylaxis should not be discontinued after immunization with PNEUMOVAX.

PRECAUTIONS: Any febrile respiratory illness or other active infection is reason for delaying use of PNEUMOVAX, except when, in the opinion of the physician, withholding the agent entails even greater risk.

Caution and appropriate care should be exercised in administering PNEUMOVAX to individuals with severely compromised cardiac and/or pulmonary function in whom a systemic reaction would pose a significant risk and also to patients who have had episodes of pneumococcal pneumonia or other pneumococcal infection in the preceding three years and may have high levels of preexisting pneumococcal antibodies which may result in increased reactions, mostly local but occasionally systemic. Available data suggest that revaccination before three years may result in more frequent and severe local reactions at the site of injection, especially in persons who have retained high antibody levels.

Children under two years of age may not obtain a satisfactory antibody response to some pneumococcal capsular types. Therefore, the vaccine should not be used in this age group. PNEUMOVAX may not be effective in preventing infection resulting from basilar skull fracture or from external communication with cerebrospinal fluid.

ADVERSE REACTIONS: Local erythema and soreness at the injection site, usually of less than 48 hours' duration, occurs commonly; local induration occurs less commonly. In a study of PNEUMOVAX (containing 14 capsular types) in 26 adults, 24 (92%) showed local reaction characterized principally by local soreness and/or induration at the injection site within 2 days after vaccination. Low-grade fever (less than 100.9°F) occurs occasionally and is usually confined to the 24-hour period following vaccination. Although rare, fever over 102°F has been reported.

Reactions of greater severity, duration, or extent are unusual. Rarely, anaphylactoid reactions have been reported.

NOTE: Administer subcutaneously or intramuscularly. **DO NOT GIVE INTRAVENOUSLY. DO NOT GIVE INTRADERMALLY.**

STORAGE AND USE: Store single-dose prefilled syringes and unopened and opened vials at 2-8°C (35.6-46.4°F). The vaccine is used directly as supplied. No dilution or reconstitution is necessary. Phenol 0.25% added as preservative.

Use a separate heat-sterilized syringe and needle for each individual patient to prevent transmission of hepatitis B and other infectious agents from one person to another. All vaccine must be discarded after the expiration date.

Single-Dose Prefilled Syringe

Inject contents of syringe to effect a single dose.

Single-Dose and 5-Dose Vials

For Syringe Use: Withdraw 0.5 ml from vial using a sterile needle and syringe free of preservatives, antivenoms, and detergents.

HOW SUPPLIED: PNEUMOVAX is supplied in 5-dose vials of liquid vaccine, for use with syringe only, in a box of 5 individual cartons, each containing a single-dose vial of vaccine; and in 5 single-dose prefilled syringes.

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For more detailed information, consult your MSD representative or see full prescribing information: Merck Sharp & Dohme, Division of Merck & Co., Inc., West Point, Pa.

Letters to the Editor

Readers are invited to submit letters for publication in this department. Submit to Doris Flournoy, Executive Editor, Journal of Occupational Medicine, 150 N. Wacker Drive, Chicago, IL 60606. Letters should be typewritten, double spaced and should be designated "For Publication."

Dose-Response and Immortality in SMR Studies

To the Editor: Because dose-response is an important criterion in the determination of causality, industrial epidemiologists often examine their standardized mortality ratio (SMR) results by level of exposure. Classification of workers into high and low categories based upon their highest exposure job is a method commonly used (see the acrylonitrile study in the April 1980, JOM for a recent example). Unfortunately, investigators using this "highest exposure job" method often make the mistake of allocating all of the person-years at risk for each worker to just one exposure category, a procedure that can negate or reverse what might actually be a positive dose-response gradient. The problem has received little attention to date, and consequently misallocation of person-years is rather common. For instance, three of nine SMR studies of vinyl chloride-exposed workers have made this error.^{1,2,3}

An example will help to illustrate the problem. Suppose there is a plant at which all workers start at the same time in low-exposure jobs, and 20 years later the process changes such that all jobs for those still working are considered high exposure (no workers enter or leave the work force, except for deaths). When the workers are subsequently classified into low and high categories on the basis of highest exposure job ever held, one finds in the low-exposure category that the number of observed deaths is much greater than the expected number, in fact all of the workers in the low exposure category are dead. However, in the high-exposure category the mortality is much less than ex-

pected, in fact nobody in the high-exposure category dies in the first 20 years after initial employment. One would conclude from such an analysis that low exposures are quite dangerous but that high exposures are somehow protective.

This fictitious example is extreme, but it serves to show that workers who move from low- to high-exposure jobs will bias results if they (and all their person-years) are classified by highest exposure job. The problem is that, for such workers, low-exposure person-years are included in the high-exposure category. These low-exposure person-years are immortal in the high category because if workers die while in low-exposure jobs, their deaths are put into the low category. The high category, therefore, contains too many person-years at risk and overestimates the expected number of deaths. The opposite occurs in the low category. The result for the high category is conservative mortality ratios and the result for the low category is inflated mortality ratios.

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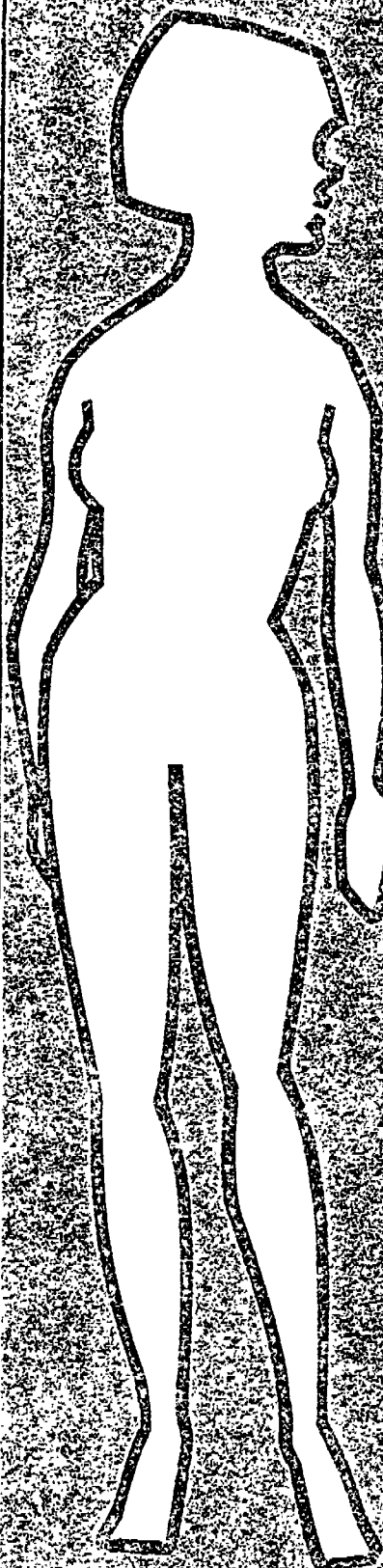
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Letters continued

A solution is to allocate person-years to the low-exposure category until workers switch to high-exposure jobs. Only when they make the job change should their person-years be allocated to the high-exposure category. This principle has previously been termed "concurrent classification" by Waxweiler.⁴ Workers who start in high-exposure jobs and change to low-exposure jobs do not require special handling, because with the highest exposure job method, all of their person-years are considered high exposure. (The method assumes that the highest exposure determines excess disease risk.)

The correct data processing requires selection of certain workers and control over the beginning and ending of person-years calculations for each worker. For the "low" computer run, workers who began work in a low-exposure job are selected. Those selected who changed to a high-exposure job have their person-years stop accumulating on the date of the job change, and the remainder (those who stayed in low-exposure jobs) are processed as usual. For the "high" computer run, all workers who were ever in a high-exposure job are selected. Those selected whose first job was a low-exposure job have their person-years start on the date of the switch to the first high-exposure job, and again the remainder (those who started in high-exposure jobs) are processed as usual. If three or more categories are desired, e.g., low, medium, and high, the analysis is more complex but is still feasible.

A final comment is that the highest exposure job method does not take into account the length of time exposed. To account for time, an alternate method of assessing dose-response is to analyze by length of exposure and to weight the time by a dose factor relating to the actual exposure level of the job (the resultant variable can be called "cumulative exposure"). But regardless of whether the "highest exposure job" or "cumulative exposure" method is used, care needs to be taken to allocate a worker's person-years at risk to appropriate exposure categories,

and not to lump all of a worker's person-years into one category.

James J. Beaumont, Ph.D.
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References

1. Fox AJ, and Collier PF: Mortality experience of workers exposed to vinyl chloride monomer in the manufacture of polyvinyl chloride in Great Britain. *Br J Ind Med* 34:1-10, 1977.
2. Equitable Environmental Health, Inc.: Epidemiologic study of vinyl chloride workers. Final report submitted to Manufacturing Chemists Association, 1978.
3. Ott MG, Langner RR, and Holder BB: Vinyl chloride exposure in a controlled industrial environment. *Arch Environ Health* 30:333-339, 1975.
4. Waxweiler RJ: Methodologic considerations in occupational cohort mortality studies. Presented at the Annual Meeting of the Society for Epidemiologic Research, 1979.

Bladder Cancer and Dairy Farming

To the Editor: A recent occupational survey from Roswell Park Memorial Institute¹ reported an association between bladder cancer and dairy farming. Although this association was not evident in other mortality surveys of farmers,^{2,3} the wide range of potentially hazardous exposures (i.e., pesticides, fuels and oils, solvents, paints, and fertilizers) used in farming plus the large population-at-risk underscores the need to further evaluate this new lead. Concern about pesticide exposure was also raised by the recent report of an excess risk of bladder cancer among pesticide applicators.⁴ Through a quick and inexpensive case-control study, we examined the occupational statements on a large number of death certificates from Wisconsin, a state with a large dairy industry.

Between 1968 and 1976 there were 1,386 deaths from bladder cancer among white males 30 years or older. For each death certificate giving bladder cancer as the underlying cause, a control certificate, matched on race, sex, age and year of death, and county of residence was chosen from other causes of death. Occupation, as recorded on the death certificate, was coded according to the 1960 Census⁵ Odds ratios (OR), as calculated by the McNemar test,⁶ significance tests, and 95% confidence