Measurement strategies to evaluate occupational exposure to pesticides

Berna van Wendel de Joode, IRET, UNA,Costa Rica

In general, to examine associations between exposures and health effects in epidemiological studies, the study population needs to comprise both healthy and ill persons with contrasting exposure levels. With respect to exposure, it is necessary to characterize duration and intensity of exposure for each study participant, or for groups of study participants with similar exposures. Yet, workers who perform the same jobs may have different exposure levels, and therefore ideally exposure should be measured. These measurement strategies should measure variability in exposure between and within persons (Rappaport et al 1995; Lyles et al 1997; Kromhout, 2002). Prior to designing the most effective measurement strategy, basic information should be collected, pilot studies maybe performed and scientific literature of similar study populations should be revised prior to performing exposure measurements.

1) Past exposure

a) Past exposure assessment data (if available)
b) Questionnaires: Generally passed exposure is assessed using questionnaires to assess
   i) Ever / never use of specific pesticides (i.e. Agricultural health study)
   ii) Total days of application during life of specific pesticides, or, groups of pesticides (e.g. Fieten et al., 2009)
   iii) Re-entry work
   iv) Use of specific pesticide at home/farms
   v) Use of Personal Protective Equipment
c) Tasks performed during life / task-exposure matrix
d) Job performed during life / job exposure matrix
e) Algorithms or exposure models to assess exposure semi-quantitatively
   i) Pesticide-specific parental exposure (Monge et al 2007)
      - Icon-based questionnaires to reduce recall bias (i.e. Monge et al 2004; Valke et al 2005)
        (a) Interviews of experts / guidelines for pesticide use / importation of pesticides to reduce recall bias (Monge et al., 2005)
   ii) Agricultural health study (Dosemeci et al., 2002);
   iii) Life-time exposure algorithm for applicators, re-entry workers (Negatu et al., 2016)
   iv) Completion of observational methods based on interviews (i.e. DREAM, DERM)
f) Pesticide poisoning (acute and high exposures)
   i) Self-report
      - Ever experienced unusually high exposure, if so, specify pesticide and mode of exposure
      - Ever intoxicated with pesticides, if so, indicate what pesticide – reported symptoms indicate severeness of poisoning
      - Ever sought medical care (clinic or hospital) for pesticide exposure, if so, specify pesticide and mode of exposure
        (a) Number of times sought medical care
      - Ever hospitalized for pesticide exposure, if so, specify pesticide and mode of exposure
      - Ever diagnosed with pesticide poisoning by a medical doctor, if so, specify pesticide and mode of exposure

ii) Validated medical record: obtain consent to abstract data from patient's medical record to document or confirm patient report of poisoning or evidence of high pesticide exposure (e.g. dermal evidence, acute respiratory condition, etc.)
    - for persons without access to medical care this results in underreporting

2) Current exposure

a) Characterization of jobs and workplace
   i) If possible, perform a visit to the enterprise to obtain data on
      - which pesticides are being applied
      - the frequency and months/season of their application
      - since when each pesticide has been used
      - if available, the concentration of active ingredient, diluted solution, and how many liters are applied per Ha (or other unit) to be able to calculate grams of active ingredient used during a certain period (for example g/Ha/year).
   ii) Document use of personal protective equipment
   iii) Document all job-titles
   iv) Observe workers when performing applications
   v) Document also exposure of possible by-standers and persons performing re-entry tasks.
   vi) Group job-titles into the ones that are expected to be exposed and not exposed.
   vii) Group job-titles according to exposure levels that are expected to be similar, for example high - medium - low
      - assign arbitrary weights to these categories that allow calculation of semi-quantitative scores (i.e. high=5, medium=3, low=1 (Loomis et al, 1994).
      - Interview workers about their work history to learn about duration of this exposure.

b) (Semi) quantitative exposure assessment at the workplace
   i) Measurement strategy - It is recommendable to
      - Randomly select workers to be observed or measured
      - observe the same workers over different days to allow the estimation of variability between and within job-titles, or between and within workers (Rappaport et al 1995; Lyles et al 1997; Kromhout 2002).
      - ideally have the sampling days at least several weeks apart to allow for a better estimate in time.
      - complete random exposure assessment with observations on specific days in case of specific tasks that are expected to result in increased exposure levels (Kromhout 2002).
   ii) With respect to pesticides, attention should be paid to dermal exposure, as for most occupational pesticide exposures, the skin is the principal route-of-entry.
   iii) Semi-quantitative measurements
      - Observational method to assess pesticide exposure can be used. For example, for dermal exposure assessment several methods are available (see Lesmes (2015) for comparison of several methods): i.e. DREAM (van Wendel de Joode et al. 2003; 2005a, b), DERM (Blanco et al 2006), or use of fluorescent tracer (Fenske 1988; Fenske and Birnbaum 1997; Aragon et al 2004, 2006). Those methods result in scores that can be used to rank, or group, workers' exposure levels. The results of the semi-quantitative methods will give input for the quantitative measurement strategy, for example, in case of dermal exposure what body parts should be measured.
   iv) Quantitative measurements
      - Measurement of home or work environment and sources of exposure

(a) Environmental air measurements
(i) Environmental air measurements tend to underestimate workers' exposure levels, as workers interact with the source of exposure
(ii) Active air sampling
(iii) Passive air sampling
(b) Drinking water
(c) Food
(d) Soil

- Personal dermal exposure assessment
  (a) Removal methods
  (i) Hand washing
  (ii) Skin stripping
  (b) Surrogate skin methods
  (i) Pads
  (ii) Gloves
- Personal air measurements
  (a) Active air sampling
  (b) Passive air sampling

v) Pesticide concentrations in biological samples

- Urine – To obtain information on current pesticide exposure, pesticide metabolite concentrations are often measured in urine. It is non-invasive and give an estimate of the total exposure resulting from different source of exposure. As metabolite of current-use pesticides generally have short half-lives, it is again important to obtain repeated samples in time.
- Other

c) Questionnaires

Questionnaires are useful to complete the information described above, or, possibly is the only source of information when direct observation is not possible.

Appendix 1 - Examples of questions

	Question	Answers	Skip		
1	Did you ever apply pesticides?	No=0 Yes=1	If 0 skip to …		
2	Did ever apply pesticides on to kill weeds	No=0 Yes=1	If 0 skip to ..		
3	Paraquat/Gramoxone/chemical to burn weeds	No=0 Yes=1	If 0 skip to 4		
3.1	How old were you when you applied it for the first time?	years			
3.2	How old were you when you applied it for last time?	years			

3.3	The number of times you used this chemical was similar during the years you used it?	No=0 Yes=1			
3.4	Period (start with most recent)	Age at start	Age at end	# Times/year[1]	Possibly add question(s) on PPE
3.5	Before that …	Age at start	Age at end		
3.5	Before that .. (etc)	Age at start	Age at end		
4	Round-up/glyphosate/systemic	No=0 Yes=1	If 0 skip to ..		

[1] if frequent interviewer converts answer to times a year; if less than once a year interviewer converts to number of times a year (i.e. once every five years is 0.2)

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