A START TOWARD MICRONUCLEI-BASED DECOMPRESSION MODELS; ALTITUDE DECOMPRESSION

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1. BIG QUESTION

What are the triggers for bubbles of decompression sickness (DCS)?

Why not develop a mathematical model based on gaseous micronuclei to see where it leads?

Altitude decompression is simpler than diving because there is no compression before decompression.

2. ASSUMPTIONS ABOUT MICRONUCLEI

- Micronuclei occur in a population of varying susceptibilities (or error, response scaling with population increase or decrease).
- Micronuclei get smaller due to outward diffusion when the subject breathes 100% oxygen before going to altitude (O_2 prebreathing).
- Micronuclei enlarge according to Boyle's law during decompression.
- After decompression, they enlarge due to inward diffusion of nitrogen from body fluids.
- Diffusive exchanges take time.
- Micronuclei are stable as they vary in size, but lose stability if they become enlarged to their "critical nucleation radius" – then they form bubbles.

3. DATASET for comparison with the model:

- 4,756 men in controlled altitude trials (Aviat Space Environ Med 1999;70(4):315-21).

Scatter is large in the two panels of Fig. 1; variables other than those plotted affect the positions of the points.

- There is almost no trend in panel A.
- In contrast, panel B shows a definite falling trend – risk decreases when the subject prebreathes 100% oxygen.

Note especially, the dotted exponential decay curve in panel B does not fit the trend. There is little effect unless O_2 prebreathing lasts more than an hour.

We infer that the direct effect of O_2 prebreathing is the shrinkage of micronuclei; the exponential washout of N_2 from tissue sets up the diffusion gradient for the shrinkage.

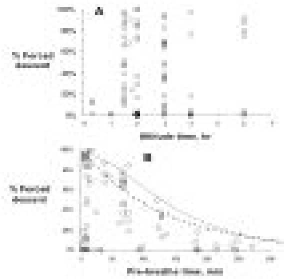

Figure 1. Percent of serious DCS plotted against two of the variables; each point represents a group of from 4 to 434 men. A, duration of altitude exposure. B, length of time before exposure that subjects breathe 100% oxygen.

4. THE MODEL

Four independent variables:

- Length of O_2 prebreathing before exposure.
- Exposure altitude.
- Duration of exposure.
- Rate of ascent to altitude.

Dependent variable:

- DCS serious enough to require descent from altitude before the planned end of the test (= forced descent).

Estimation of parameters:

- By trial and error aided by maximum likelihood statistical analysis.

Structure of the model

Probability of forced descent = $1 - e^{-aRc}$

- a = parameter
- Rc = cumulative risk, the product of risks due to the four independent variables

Risks for the variables are entered into the model as distribution functions:

- The assumption here is that risk will cause micronuclei from the underlying population to nucleate into DCS bubbles.
- Conversely, O_2 prebreathing will cause fewer nucleations.

5. MODEL PREDICTIONS

Figure 2 shows the scatter of data points around the line of identity – not bad for data from various sources.

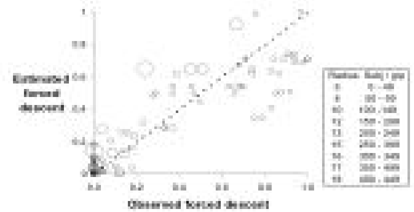

Figure 2. Accuracy of model predictions. Areas of the points give an idea of the number of subjects in the groups.

For Fig. 3, we divided the dataset into three subsets at low, medium, and high percentage of forced descent DCS.

- The curves in Fig. 3 fall near the averages for the subdivisions of the data.
- The S-shaped curves reflect the assumed distribution functions.

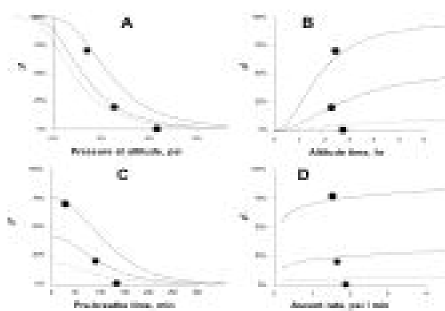

Figure 3. Curves are predictions of the model for three subdivisions of the dataset: high, medium, and low risk. Black points show averages for the subdivisions.

6. POPULATIONS OF MICRONUCLEI vs. DCS

The curves in Fig. 3 show the percentage of subjects who suffer forced-descent symptoms of DCS. Assume that the curves also reflect the number of micronuclei that become bubbles in one subject; more bubbles means more chance of DCS.

- If altitude pressure is very low, enough micronuclei can nucleate to cause 100% chance of forced descent symptoms, no matter how great the risk due to other variables is (Fig 3A).
- Enough micronuclei can nucleate to give 100% chance of forced descent when altitude times are very long and risk due to other variables is high (Fig. 3B).
- There is a limit to how many micronuclei can nucleate when risk due to other variables is medium or low, no matter how long the altitude time is (Fig. 3B).
- As prebreathing time increases, fewer and fewer nucleations occur (Fig. 3C); after 300 min, none nucleate no matter how great the risk due to other variables is. We infer that prebreathing of O_2 either destroys micronuclei or makes them too small to nucleate.
- Risk due to ascent rate tends to level off at low rates (Fig. 3D).

7. CONCLUSIONS

In this project, the lay of the data points vs. prebreathing time in Fig. 1B is the best evidence that populations of micronuclei are involved in DCS.

Major points:

- We infer that rising DCS rate with increase of the risk variables is due to recruitment of micronuclei from the population.
- Susceptibility to nucleation varies in the population of micronuclei giving the curves in the Fig. 3 plots.
- Increases of altitude can lead to 100% DCS, no matter what the other risks are, but the same cannot be said for length of exposure or rate of ascent.
- The data indicate that prebreathing's effect is due to depression of nucleation, and not directly due to tissue denitrogenation.