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QUANTITATIVE INTERPRETATION OF IMMUNE TEST RESULTS IN ATHLETES

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KEY WORDS: illness, athlete, statistics, reference range, variability

Effective use of immune system profiling or monitoring in athletes requires a carefully designed and implemented program. A program to improve athlete health typically comprises clinical support, education of athletes, coaches and officials, training management, dietary practices, and occasionally biomedical or immune testing. From a quantitative perspective, the primary issues in interpreting an immune test with confidence include reference ranges, the smallest worthwhile change or difference, and various statistical terms. In relation to likely clinical outcomes, clinicians and researchers also need basic knowledge on interpreting odds ratios, risk ratios and hazard ratios. In a research setting there are choices of various analytical approaches from traditional statistical significance, to Bayesian analysis, and other hybrid approaches.

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REFERENCE RANGES

A long-standing issue with clinicians and researchers is the availability of sports-specific reference range intervals for haematological, biochemical and immunological measures in athletic populations. The extent to which sports-specific ranges vary in comparison with standard clinical reference values, is unclear. Prospective longitudinal studies are needed to develop sports-specific reference ranges for clinicians in diagnostic and screening settings, and assist researchers clarify the effects of various training, lifestyle, and dietary interventions, and changes in inflammatory control processes. Encouragingly, some preliminary work has been useful in identifying differences in cell counts and markers between sports⁽¹⁾.

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SMALLEST WORTHWHILE CHANGE OR DIFFERENCE

When interpreting changes in an athlete's immune profile it is important to determine the magnitude of the smallest clinically important change in the immune parameter(s) of interest, and the likely uncertainty or noise in the test result. Where no direct relationship between the risk of illness and biomarker concentration has been established, an appropriate default approach is one-fifth of the between-subject standard deviation (a standardised or Cohen effect size of 0.20). Uncertainty or noise in a test result is best expressed as the typical or standard error of measurement derived from a reliability study. The noise in quantifying many cellular and soluble immune parameters is often greater than the smallest worthwhile difference, so assessment of changes in the risk of illness can be problematic. Unrealistically large changes can be partially discounted when tests are noisy.

STATISTICAL TERMS

In the context of sports medicine, test sensitivity can be defined as the ability of a test to correctly identify those with illness or infection (true positive rate), whereas test specificity refers to the ability of the test to correctly identify those without illness (true negative rate). Interpreting the variability in immunological markers within and between athlete cohorts can be informative. For example, the variability and fluctuation of salivary immunoglobulin concentrations can be consistently greater in elite swimmers, but multiple samples from individual swimmers were less correlated compared with participants with lower physical activity levels⁽²⁾. These outcomes have implications for monitoring mucosal immune status within individuals, and when comparing salivary immunoglobulin concentrations between groups with differing levels of physical fitness and activity.

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ODDS, RISK AND HAZARD RATIOS

The risk ratio (or relative risk) is the ratio of the risk of illness in two groups (for example a group of athletes presenting with illness and a second group of healthy counterparts), whereas the odds ratio is the ratio of the odds of an event. For both measures, a value of 1 indicates that the estimated effects are the same for both interventions (groups). The hazard ratio is defined as the ratio of the hazard rates corresponding to the conditions described by two levels of an explanatory variable. For example, in an athlete study of training loads and illness, an over-trained group may experience upper respiratory illness at twice the rate per unit time as the control group. The hazard ratio would be 2, indicating higher

hazard of illness from overtraining. Or in another study, female athletes undertaking the same training may suffer from illness three times more frequently per unit time than men, giving a hazard ratio of 3. Hazard ratios differ from relative risks and odds ratios in that the latter two are cumulative over an entire study, using a defined endpoint, while hazard ratios represent instantaneous risk over the study time period.

Various measures of illness incidence in athletes include illness risk (proportion of athletes with illness in a given period of training or competition), illness rate (number of illnesses per unit of training), odds of illness (probability that illness will occur divided by probability that illness will not happen), and mean time or mean number of sessions or games to illness. Effects of risk factors are estimated as values of effect statistics representing differences or ratios of one or more of these measures between groups defined by the risk factor. Values of selected ratios and their sampling uncertainty (confidence limits) are estimated with specialised procedures: odds ratios with logistic regression, rate ratios with Poisson regression, and hazard ratios with proportional hazards (Cox) regression⁽³⁾. Illness risks and mean time to illness in different groups can also be estimated and often give a better sense of the effect of a risk factor.

STATISTICAL APPROACHES IN RESEARCH STUDIES

The choice of analytical approach for research has generated lots of academic debate. While most clinicians and researchers are taught the basics of statistical significance at university, limitations of significance or hypothesis testing have been well documented⁽⁴⁾. Researchers should have a basic understanding of the shortcoming and misuses of significance testing and improper handling of p-values. Appropriate interpretation of study results should include estimates of magnitudes and precision of estimation (confidence limits). In some ways this choice can be simplified down to frequentist versus Bayesian analysis, although in sports science there has been much debate about the emergence of other non-Bayesian or magnitude-based inference approaches⁽⁵⁾. The merits of these approaches is beyond the scope of this article, although suffice to say that analytical approaches for small sample studies (often the case in human experimentation) using full Bayesian, quasi-Bayesian and frequentist decisions must be well justified, reported transparently and interpreted correctly.

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PRACTICAL IMPLEMENTATION

Practical implementation of research paradigms in the field with athletes and sports is often a challenge. Our research group developed a model of salivary IgA concentration as

a marker of the risk of upper respiratory tract illness during the 1990's⁽⁶⁾. Although there is still merit in this approach with athletes, implementation has proved challenging in the field. A substantial number of studies have been published on exercise and salivary IgA, and variable outcomes can dilute confidence in interpreting results. Difficulties in standardisation of specimen collection, storage and handling of samples, and laboratory- and field-based quantification are often experienced⁽⁶⁾. Moreover, the cost of biomedical testing is significant for many sports and nations. Diagnostic testing still forms the majority of work, although technological advances and further research should facilitate an increase in monitoring and intervention before athletes present with symptoms of illness. The advent of small portable point-of-care analysers is promising. However, researchers, clinicians and team support personnel have to be mindful of calibration, reliability and validity of instruments irrespective of their size and portability. Translation of quantitative algorithms and references ranges, and how those values might vary between field and laboratory settings are current research foci.

REFERENCES

1. Horn, P. et al. (2010), "Lower white blood cells counts in elite athletes training for highly aerobic sports", *Eur J Appl Physiol* Vol.110 Ch. 5, pp. 925-32.
2. Francis, C.L. et al. (2004), "Variation of salivary immunoglobulins in exercising and sedentary populations", *Med Sci Sports Exerc*, Vol. 37, Ch. 4, pp. 571-8.
3. Hopkins, W.G. et al. (2007), "Risk factors and risk statistics for sports injuries" *Clin J Sport Med*. Vol. 17, Ch.3, pp. 208-10.
4. Stang, A. et al. (2011), "The ongoing tyranny of statistical significance testing in biomedical research, *Eur J Epidemiol*. Vol. 25, pp. 225-230.
5. Mengersen, K. et al. (2016), "Bayesian Estimation of Small Effects in Exercise and Sports Science" *PLoS One*. Apr 13, Vol. 11, N°4 e0147311.
6. Gleeson, M. Pyne, D.B. (2016), "Respiratory inflammation and infections in high-performance athletes", *Immunol Cell Biol*. Vol. 94, Ch. 2, pp. 124-31.