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17 **Scientific Progress or Regress in Sports Physiology?**

18 *Invited Commentary*

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34 **ABSTRACT**

35

36 In modern societies there is strong belief in scientific progress. But unfortunately a parallel
37 partial regress occurs because of often evitable mistakes. Mistakes are mainly forgetting,
38 erroneous theories, errors in experiments and manuscripts, prejudice, selected publication of
39 “positive” results and fraud. An example for forgetting is that methods introduced decades
40 ago are used without knowing the underlying theories: basic articles are no longer read nor
41 cited. This omission may cause incorrect interpretation of results. For instance false use of
42 actual base excess instead of standard base excess for calculation of the number of hydrogen
43 ions leaving the muscles raised the idea that an unknown fixed acid is produced additionally
44 to lactic acid during exercise. An erroneous theory led to the conclusion that lactate is not the
45 anion of a strong acid but a buffer. Mistakes occur after incorrect application of a method,
46 exclusion of unwelcome values, during evaluation of measurements by false calculations, or
47 during preparation of manuscripts. Coauthors as well as reviewers do not always carefully
48 read papers before publication. Peer reviewers might be biased against a hypothesis or an
49 author. A general problem is selected publication of positive result. An example of fraud in
50 sports medicine is the presence of doped subjects in groups of investigated athletes. To reduce
51 regress it is important that investigators search both original and recent articles on a topic,
52 and examine conscientiously the data. All coauthors and reviewers should read the text
53 thoroughly and inspect all tables and figures in a manuscript.

54 Key words: forgetting, erroneous theories, mistakes in experiments and manuscripts, selected
55 publication, fraud

56

57 In modern societies there is strong belief in scientific progress. But unfortunately a parallel
 58 partial regress in scientific publication including sports physiology can occur because of
 59 often evitable mistakes. These errors are mainly forgetting or oversights, erroneous
 60 theories, mistakes in experiments and manuscripts, selected publication of “positive”
 61 results, prejudice, and fraud. Some mistakes can be detected by a careful reader, while other
 62 mistakes need special expertise to identify or clarify.

64 In this contribution typical examples detected by the author in the area of sports physiology
 65 are presented.

66

67 **Forgetting**

68 Often basic articles for methods introduced decades before are no longer read or cited. Also
 69 modern apparatus present “ready-made” results which formerly had to be calculated step-by-
 70 step. Without knowledge of the underlying theories incorrect interpretation of results may
 71 occur. In the following I describe some typical examples.

72 **Base excess:** False use of actual base excess (derived from blood titration with acid and base
 73 in vitro) instead of standard base excess (corrected for in vivo conditions, i.e. considering the
 74 equilibration of blood with the interstitial fluid) for quantifying the number of hydrogen ions
 75 leaving the muscles raised the idea that an unknown fixed acid is produced additionally to
 76 lactic acid during hard exercise.¹ In contrast the decrease of standard base excess fits well to
 77 the increase of [lactate].^{2,3}

78 **Efficiency:** Gross efficiency during cycling has been compared in untrained and trained
 79 subjects for equal percentages of maximal power without considering its dependence on
 80 metabolic rate and pedal rate. This shortcoming led to the belief (in contrast to the classical
 81 opinion) that metabolic efficiency can be markedly improved by training.⁴⁻⁶ Fig. 1 from
 82 Böning et al.⁷ shows that gross efficiency (upper panel) changes with absolute power
 83 (because the relative contribution of basal metabolism to total energy consumption decreases
 84 with power) and pedal rate (mainly because of the changing contribution of idling). There is
 85 only a small overall difference between untrained and trained subjects. Net efficiency also
 86 varies with pedal rate (lower panel), but the maximal value is independent of power; training
 87 most likely has no significant effect. Therefore comparisons are only valid if these simple
 88 facts are considered.

89 Often efficiency is even not calculated but decreases in oxygen uptake are taken as proof
 90 for an improvement, e. g. during an altitude stay⁸ or after intake of nitrate in form of
 91 beetroot juice.⁹ But for a correct calculation of energy turnover the consideration of CO₂
 92 production is also necessary to determine the relation of fat and carbohydrate consumption
 93 by use of the respiratory exchange ratio.¹⁰ Altitude acclimatization causes a reduction in fat
 94 combustion!¹¹ Strangely in spite of routine measurement of both O₂ and CO₂ in modern
 95 equipment this calculation is often omitted. An additional possible mistake is to neglect
 96 anaerobic metabolism which plays a role at intensities above the maximal lactate steady
 97 state.¹²

98 **Literature Searches:** Relevant articles are not always found. In former years scientists
 99 mainly relied on their institutional library collections which never were complete; e. g. some
 100 important European journals were not present in American universities and vice versa. Today
 101 most researchers search references in PubMed, which also presents only a selection of
 102 scientific journals. Additional use of Google scholar and other sources is helpful.

103

104 **Erroneous Theories**

105 Robergs et al.¹³ proposed in 2004 that lactate is not the anion of a strong acid but a buffer.
 106 Besides using a new controversial concept of “metabolic buffering” the apparently
 107 supporting calculations (number of liberated H⁺, muscular buffer capacity) were erroneous.
 108 ^{2,14}

109 The widely accepted theories of Peter Stewart (e. g. described in^{15,16}) are partly based on a
 110 conceptual error. He and his followers consider a balance equation of cation and anion
 111 concentrations, characterized by the equality sign, e. g.

112 $[Na^+] + [K^+] + [H^+] = [Cl^-] + [HCO_3^-] + [OH^-]$

113 like a chemical reaction equation, characterized by a flash, e. g.

114 $HCl \rightarrow H^+ + Cl^-$

115 and thus return to concepts (e. g. Cl⁻ considered as an acid) already abandoned at beginning
 116 of the 20th century.² Additionally the large number of measured electrolyte concentrations in
 117 plasma and red cells cause scattering and make practical application laborious. Therefore I
 118 myself did not publish similar measurements during respiratory acidosis and alkalosis in
 119 man.

120

121 **Mistakes in Experiments and their Evaluation**

122 Mistakes may occur after incorrect application of a method, during evaluation of
 123 measurements, by false calculations, or exclusion of unwelcome values (extreme values
 124 sometimes point to subjects with unexpected properties). In the following section I describe
 125 examples mainly from own investigations. Some examples (mainly from own
 126 investigations) are useful for illustrating common mistakes.

127

128 **Discarding of “improbable” results.** Head-out immersion causes diuresis, but the effect is
 129 reduced in endurance-trained athletes.¹⁷ Therefore some athletes could not void every 30 min
 130 in our experiments. The student performing the measurements originally discarded all zero
 131 values thus eliminating the significance of the training effect.

132 Moreover single outliers are not always caused by measurement or evaluation errors but may
 133 be indicative for a special biologic effect. **Ende Durchsicht**

134 In subjects with cystic fibrosis a slightwards right shift of the standard oxygen dissociation
 135 curve of hemoglobin (measured as increase of the half saturation pressure P₅₀ at 40 mmHg

136 PCO₂, pH 7.4, 37°C) is generally observed.¹⁸ A statistically confirmed outlier in the patients
 137 (Fig. 2) is no measurement error, but caused by low 2,3-biphosphoglycerate concentration.
 138 This points to an optimal adaptation for combined hypoxia-hypercapnia in this patient,
 139 because binding of O₂ to blood in the lungs is facilitated. Moles living under similar
 140 conditions inspiring air with reduced O₂ and increased CO₂ content are perfectly adapted
 141 possessing a low standard P₅₀.¹⁹ Interestingly in other publications on cystic fibrosis similar
 142 outliers can be detected.

143 Similarly at altitude the typical but not optimal human acclimatization reaction is a rightward
 144 shift of the standard oxygen dissociation curve in contrast to a leftward shift in well-adapted
 145 animals like llamas. But “human llamas” have been detected occasionally.^{20,21} An interesting
 146 example for an outlier is also the famous mountaineer Reinhold Messner.^{22,23} He reached an
 147 arterial oxygen saturation of nearly 93% during exercise (90 W, ventilation 34.4 l/min) in
 148 artificial hypoxia (inspiratory PO₂ 77 mmHg corresponding to 5500 m of altitude). In contrast
 149 5 other mountaineers ventilated approximately 41 l/min, but showed average saturations of
 150 only 72%. Messner’s high saturation can only be explained by a low half saturation pressure
 151 like in llamas – or a leak in the system. Unfortunately I lost the reference with his data years
 152 ago and I hesitated too long to contact him for some measurements (blood gases and acid
 153 base status, BPG metabolism, Hb type). Now (age 71 years) he is not willing to take part.

154

155 **“Responders” and “Nonresponders”.** Chapman et al.²⁴ have grouped athletes after altitude
 156 training according to their improvement in running time. Athletes with performance
 157 improvements better than the mean value were called responders, runners without
 158 improvement were called nonresponders, the rest was omitted. Consequently after this
 159 manipulation changes in erythropoietin concentration and total red cell volume were
 160 significantly different between responders and nonresponders. With this evaluation technique
 161 not extreme but intermediate values are excluded. It appears a scientist can produce herewith
 162 a s of significant effects, but are they real?

163

164 **False calculations.** The concentration of lactate is higher in plasma than in erythrocytes for
 165 three reasons: 1) lactate is present only in the water space which amounts to approximately
 166 70% in the cells, 2) the distribution of lactate is controlled by a Donnan equilibrium with
 167 lowered anion concentrations in the cell water, 3) transport by monocarboxylate channels
 168 needs several minutes until equilibrium. Comparing results of different investigations
 169 without considering these issues may lead to erroneous conclusions.^{25,26}

170

171

172 **Mistakes in Manuscripts**

173 Astonishingly coauthors as well as reviewers do not always carefully read the papers before
 174 submission and publication. For example the striking difference between leg O₂ delivery and
 175 the product CaO₂ x leg blood flow (both values must be equal) in the same table was missed
 176 by the authors²⁷ causing contrasting interpretations about erythropoietin effects. Fortunately

177 the mistake was corrected after a letter to the editor.^{28,29} As an example of various mistakes
178 in an otherwise excellent publication examining the influence of erythropoietin on maximal
179 O₂ consumption in mice³⁰, the animals had a resting heart rate of 514/min but 160/min at
180 exhaustion. Only the resting value seems to be correct because it is negatively correlated to
181 body mass in mammalia; during exercise heart rate rises usually in mice as in other animals.
182 None of 7 authors had seen this error and various other mistakes. Surprisingly the
183 corresponding regression equations yielded realistic values.³¹ Also surprisingly the journal
184 did neither accept a letter to the editor nor publish a correction.

185

186 **Selected publication of “positive” results**

187 This problem is difficult to solve. It is most important in pharmacological studies, where
188 negative results are frequently “forgotten”. But generally neither authors nor editors like
189 experiments without the expected effect. As a countermeasure a Journal of Negative Results
190 in Biomedicine has been founded.

191

192 **Prejudice**

193 The problem is demonstrated by a citation:

194 “All peers are equal, but some peer reviewers are more equal than others.”

195 (George Orwell 1945 modified) and a comic (Fig. 3). The reviewer should check
196 manuscripts for importance, clarity, completeness and mistakes. The style for different fields
197 and journal prescriptions is mainly a matter of personal taste. The frequency of inappropriate
198 reviewer comments is often increased if the reviewer is not a real expert for the topic.

199

200 **Fraud**

201 An example especially of fraud in sports medicine is the presence of doped subjects in a
202 group of investigated athletes. Thus artificially changed performance or physiological
203 variables might be considered as normal. It is necessary to be aware of this when selecting
204 subjects for scientific project. A related problem is that athletes taking part in a scientific
205 project involving prohibited substances (e. g. EPO injections) cannot go to competitions
206 before any effect has disappeared. These questions have been discussed recently.³³⁻³⁵

207

208 **Conclusions**

209 To reduce regress in physiological and performance studies it is important that investigators
210 search not only for recent articles on a topic, examine conscientiously the data and ensure
211 that all coauthors read both the text thoroughly and check tables and figures in a manuscript.
212 Reviewers have the same obligations. Journals should repeatedly invite readers to submit

213 letters to the editor for clarification which is best possible immediately after publication.
214 Frequent open discussions about important topics are essential.

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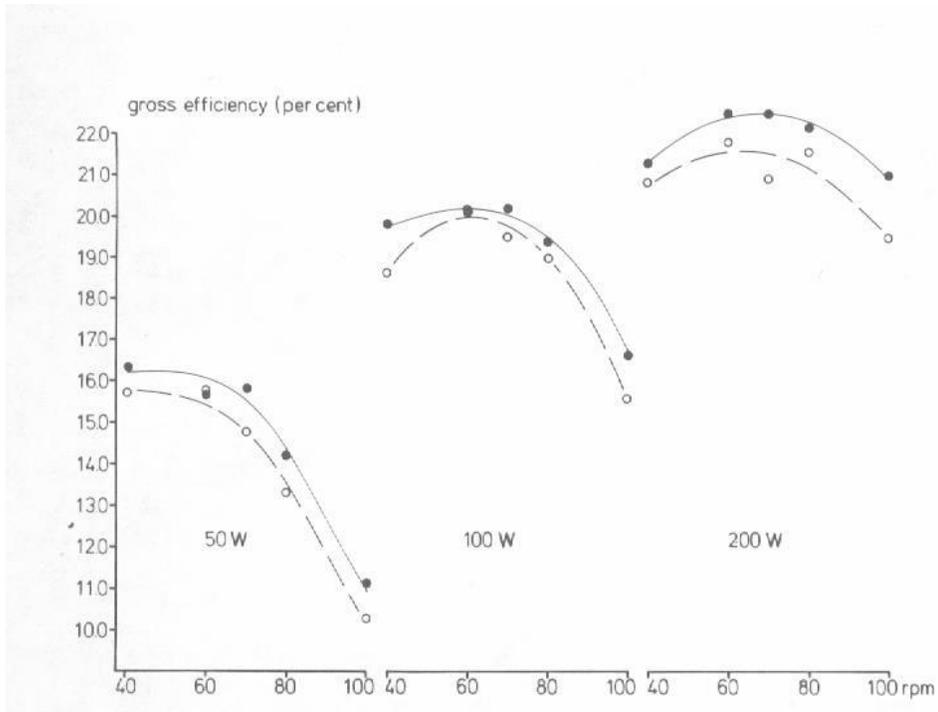
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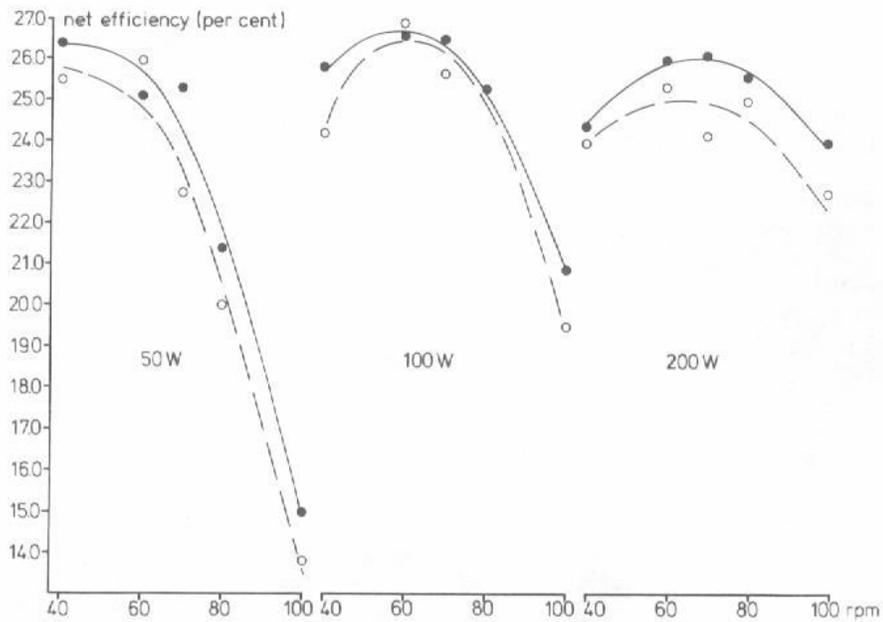
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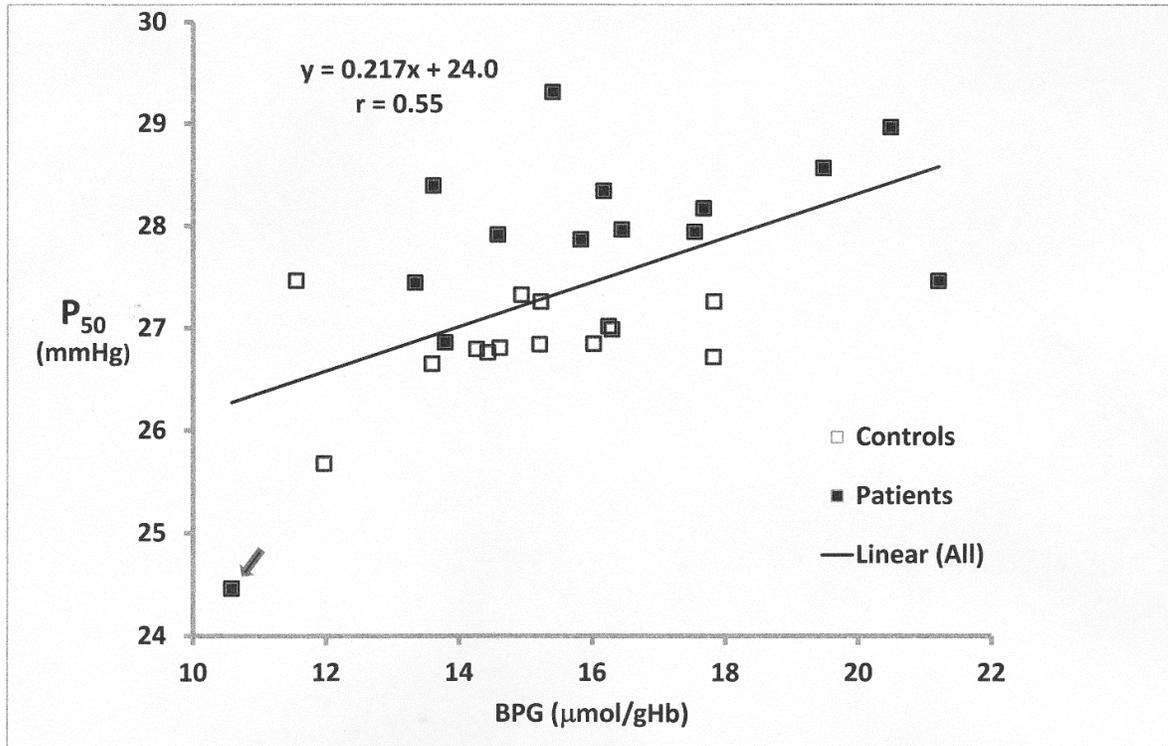
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Fig. 1. Gross (upper panel) and net (lower panel) efficiency in dependence on work load and pedal rate (rpm) in untrained (empty circles) and trained (filled circles) males. From Böning et al. (1984)⁷ with permission.

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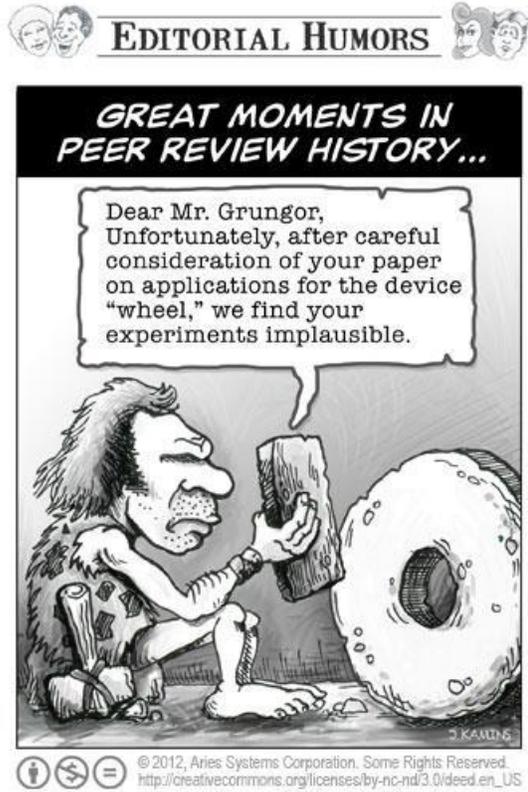




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314 Fig. 2. Standard half saturation pressure (P₅₀ at 40 mmHg PCO₂, pH 7.4, 37°C) in patients
 315 with cystic fibrosis and healthy controls in dependence on 2,3-biphosphoglycerate (BPG)
 316 concentration. One patient's value (arrow) is very low (24.4 mmHg). From Böning et al.
 317 (2014)¹⁸ with permission.



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319 Fig. 3. Peer reviewing since the Stone Age (from Aries Systems Corporation with
320 permission, http://creativecommons.org/licenses/by-nc-nd/3.0/deed.en_US).

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