Mathematic Coupling of Data

A Common Source of Error

JOSEPH P. ARCHIE, JR., PH.D., M.D.

The relationship between two variables may be mathetmatically coupled if either one or both variables are derived and/or calculated, and this can lead to erroneous results and invalid conclusions. The purpose of this report is to identify four types of mathematic coupling of data. Type 1 coupling involves directional changes in two variables which are mathematically coupled. Type 2 coupling is the functional relationship between two calculated variables which have one or more common component variables. Type 3, the most common type of mathematic coupling, is direct algebraic coupling between two variables, when one or more of the variables is derived and/or calculated. Type 4 is indirect coupling or physiologic coupling. The common problem in each type of mathematic coupling is that one variable either directly or indirectly contains the whole or components of the second variable. Statistical techniques, when properly applied to the relationship between the two variables, further obscure the underlying mathematic coupling, and tend to support the erroneous results. Recognition of mathematic coupling is imperative for correct data analysis and accurate interpretation.

SEVERAL AUTHORS HAVE IDENTIFIED and emphasized misuse of and errors in statistical techniques when applied to clinical and laboratory data.[1,2] An equally important and totally overlooked source of error in surgical and medical investigation is mathematic coupling of data. Usually mathematically coupled data is properly treated statistically, and this tends to support erroneous results and obscure the unrecognized underlying mathematic coupling. This report identifies the cause of common mishaps in mathematic data manipulation, including the most common type—algebraic coupling of calculated variables, that lead to misinterpretation of results and erroneous conclusion. Herein published examples of mathematic coupling are cited to illustrate and elucidate each type. However, it is not the intent or purpose of this study to criticize authors or editors.

Reprint requests: Joseph P. Archie, Jr., M.D., Department of Surgery, Norwood Clinic, 1529 North 25th Street, Birmingham, Alabama 35234.

Submitted for publication: October 15, 1980.

From the Departments of Surgery, Carraway Methodist Medical Center and Norwood Clinic, Birmingham, Alabama

Methods

Definitions

Mathematic coupling. Mathematic coupling means that part of the relationship between two variables that is due to a common component, where one of the variables is contained in the other variable or a third dependent variable is common to both variables.

Dependent variable. A dependent variable can take on an array of values and depends on one or more of the four classical independent variables of physical science (the three co-ordinates defining the variable's position in space, and time). Dependent variables usually have a functional relationship with one or more other dependent variables, and it is these relationships which make up the vast majority of physical science. For example, blood pressure is a dependent variable, its value depending on the instant of time in which it is measured and the position in the arterial or venous system that one measures it. Thus, it depends on the independent variables of time and position. However, blood pressure is also a function of two other dependent variables, the resistance of the vascular bed and cardiac output.

A dependent variable may be a measured variable, such as directly measured blood pressure or blood flow, or a calculated variable. A derived variable such as vascular resistance is always calculated but a calculated variable is not necessarily derived. In many instances a variable may be either measured or calculated. For example, cardiac output can be measured directly by the indicator dilution technique, or calculated from Fick measurements of oxygen consumption divided by the arterial–venous oxygen content difference.

0003-4932/81/0300/0296$00.90

Physiologic coupling. Physiologic coupling between two dependent variables means that there is a common component variable upon which both depend. However, physiologic coupling between two variables does not require that one or both variables be calculated.

Types of Mathematic Coupling

An analysis of four types of mathematic coupling that appear in the surgical and medical literature is given. The first type of mathematic coupling considered is an analysis of the directional changes in two variables which are coupled mathematically. The second type is the relationship between two calculated variables which have common component variables, and the mathematic relationship between the two variables is such that one or more of the apparent common dependent variables cancel out. The third type of mathematic coupling is direct algebraic coupling between two variables when one is derived and/or calculated. This is by far the most common type of mathematic coupling and several subtypes are given. Algebraic coupling between two variables produces an apparent correlation between the variables when no true correlation exists, or it erroneously strengthens any true functional dependence that does exist. The fourth type presented is physiologic coupling.

Results

Type 1 Mathematic Coupling

Directional changes in mathematically coupled variables. Consider a study where two variables A and B are either directly measured or calculated. A third variable C is formed from the sum of A and B. The variables of interest are A and C where C = A + B. If the question is asked, what happens to the directional changes of A and C with an intervention that affects both A and B?, then it is apparent that there are only eight possible combinations of directional change in A and C. Table 1 gives the eight combinations of either increasing or decreasing A in combination with increasing B, holding B constant, or decreasing B. Holding A constant is not considered because this does not cause a directional change in both variables. Of the eight combinations of directional changes, six are in the same direction, *i.e.*, either both A and C increase or both A and C decrease. The other two combinations are changes in A and C in opposite directions. Two sets of data of precisely this type have been recently published,[3] where 12 measurements were made in man of A and B and directional changes in A and C calculated (C = A + B). When a nonparametric statistical technique (chi square) was applied to this data the null hypothesis assumed was that there is an equal chance for A and C to go in the same and in different directions, that is, six in the same direction and six in the opposite directions. The probability values for the likelihood of the observed directional changes of Figures 2 and 3 of Rhodes et al.[3] being signficant were 0.05 and 0.01, respectively. However, because of mathematic coupling of the calculated variable C with the variable A the null hypothesis is not six and six (one to one) but rather nine and three (three to one) (Table 1). If a chi square analysis is repeated on the published data,[3] using the correct null hypothesis there is no statistical significance in direction change in either set of data. In fact the two sets of calculated data[3] were nine and three, exactly what is predicted by chance alone, and 11 and one; which is not statistically different from the correct null hypothesis for 12 measurements. The proper statistical test was applied, but the unrecognized error was produced through mathematic coupling of the variables A and C.

TABLE 1. *Directional Changes in Two Coupled Variables A and C Where A and B are "Measured" Variables and C is Calculated from C = A + B*

	Directional Change in Measured Variables A and B	Directional Change in Coupled Variables A and C	
1.	A ↑ B ↑	A ↑ C ↑	same
2.	A ↓ B ↓	A ↓ C ↓	same
3.	A ↑ B ↓, $\Delta A > \Delta B$	A ↑ C ↑	same
4.	A ↑ B ↓, $\Delta A < \Delta B$	A ↑ C ↓	different
5.	A ↓ B ↑, $\Delta A > \Delta B$	A ↓ C ↓	same
6.	A ↓ B ↑, $\Delta A < \Delta B$	A ↓ C ↑	different
7.	A ↑ B unchanged	A ↑ C ↑	same
8.	A ↓ B unchanged	A ↓ C ↓	same

Type 2 Mathematic Coupling

The functional relationship between two calculated variables with common component dependent variables. The effect of interventions that change a component of two calculated variables may be misinterpreted as a change in the relationship between the two calculated variables unless the algebraic relationship between the two calculated variables is clearly understood. Common component variables may cancel out of the mathematic relationship when two calculated variables are compared. An example of this type coupling is a recent report of the effect of partial hepatectomy on the hepatic uptake of glucagon and insulin.[4] The hepatic uptake of a substance is defined as the flux of the substance in the portal vein plus the flux of the substance in the hepatic artery minus the flux in the hepatic vein all divided by the weight of the liver. Thus an intervention such as partial hepatectomy

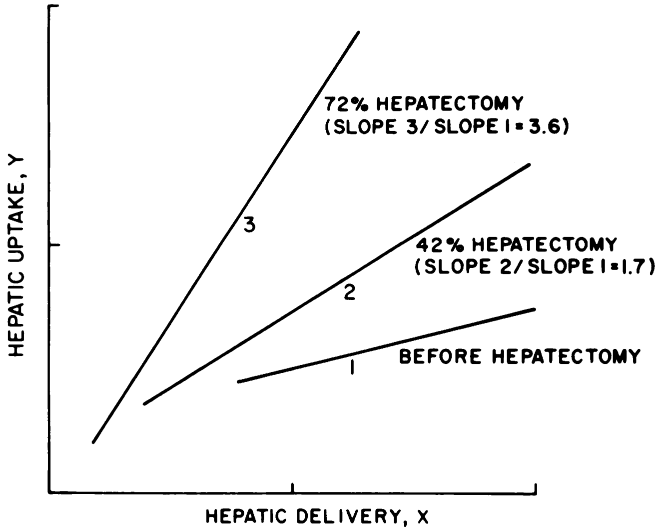

FIG. 1. Type 2 mathematic coupling. The functional relationship between two complex calculated variables is determined almost entirely by hepatic weight.

which changes the liver weight automatically changes the calculated hepatic uptake of that substance. Hepatic delivery of a substance is the flux of the substance in the portal vein plus the flux in the hepatic artery all divided by the total body weight. If one compares hepatic uptake (Y) to hepatic delivery (X), as done by Caruana and Gage[4] in their Figure 3 for insulin and Figure 4 for glucagon, the linear equation relating the two variables is $Y = aX + b$, where a is the slope and b the intercept of the line. However, direct algebraic calculation of hepatic uptake (Y) versus hepatic delivery (X) from the definition of each shows that the slope is determined almost entirely by change in the liver weight. Specifically, the equation of the line relating hepatic uptake (Y) and hepatic delivery (X) is: Y = (body weight/hepatic weight) X— (hepatic vein flux/liver weight). The slope of this line is body weight divided by liver weight. The portal vein and hepatic vein fluxes cancel out completely and are not part of the functional relationship of X and Y. The slope of the linear relationship between these two variables is determined only by body weight divided by liver weight. This is due to coupling of the calculated X and Y variables. Since the effect of removing even 72% of the liver decreases body weight only a small per cent, the change in slope of the relationship between X and Y is almost completely determined by change in liver weight, and is independent of all fluxes. Thus, no flux measurements need to be made to predict the effect of hepatectomy on the change in the slope of the relationship between hepatic uptake and hepatic delivery of a substance. The effects of a 42% and a 72% hepatectomy on these two variables are predicted independent of any experimental data and are illustrated in Figure 1. The slope of the new regression line after 42% hepatectomy is expected to have a ratio of 1.7 to 1 when compared with the original slope, and for a 72% hepatectomy the slope change is expected to be 3.6 to 1 when compared with the original slope. Figures 3 and 4 of Caruana and Gage[4] indicate a slope change after hepatectomy of 1.8 to 1 for both glucagon and insulin analysis (the expected value due to coupling of 1.7 is not significantly different), and with 72% hepatectomy the ratio was 4.1 to 1 for glucagon and for insulin 5.7 to 1 (the expected value being 3.6 to 1). Neither of the latter differences are statistically significantly different from the expected. Clearly, the published data[4] is the effect of changing liver weight (partial hepatectomy), not any metabolic changes in the liver. The results are predictable without measurements, are independent of metabolic fluxes, and, therefore, cannot be interpreted as having anything to do with insulin or glucagon being involved with hepatic regeneration as the authors suggest.[4] The linear regression analysis was applied properly but what should have been tested was the mathematic relationship between the two calculated variables hepatic uptake and hepatic delivery.

Type 3 Mathematic Coupling

Classical algebraic coupling of two variables. This type of mathematic coupling is frequently found in the literature. It occurs by addition, subtraction, multiplication, or division of one variable by another variable.

Consider a measured variable, X to which a random number, a, is added or subtracted to form a second variable $Y = X \pm a$. If one plots on a vertical axis (ordinate) the calculated variable $Y = X \pm a$ and on the horizontal axis (abscissa) the value of X, then a strong relationship between the Y co-ordinate and X coordinate is guaranteed because of coupling. Classical examples of data produced by addition and subtraction coupling are Figure 1 of Archie.[5] Figure 2 of Gale et al.,[6] Figure 1 of Fuller et al.[7] and Figure 5 of Scharf et al.[8] In each example cited the Y variable equals the X variable plus or minus some other measured variable or number. Thus, when a regression analysis is applied to the data, it is expected to be highly significant because of coupling. While there may be some true functional relationship between the X and Y variables it is clearly obscured by the strong linear X and Y mathematical coupling.

The most common type of mathematic coupling is the relationship between a measured and a calculated variable when the calculated variable equals the measured variable multiplied times another number or

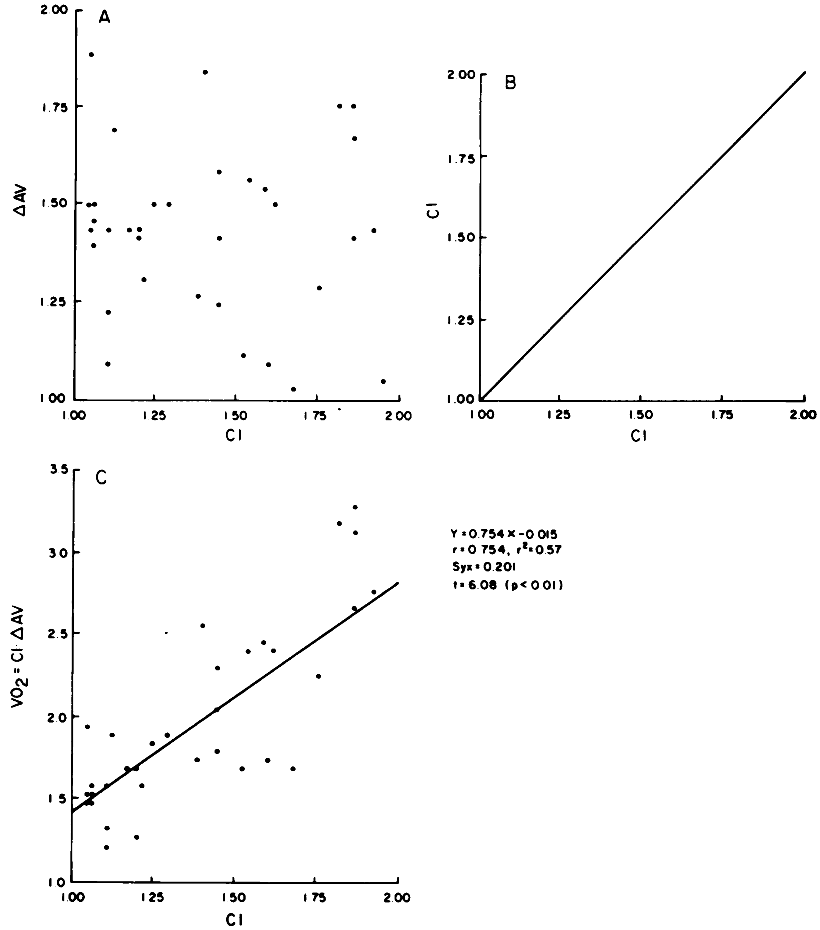

FIG. 2. Classical product coupling of variables. Arterial–venous oxygen content difference (Δ AV, Y axis) and cardiac index (CI, X axis) are the assumed measured variables given in (A), where the data was obtained from random number tables. Oxygen consumption (VO_2) is calculated from the product of cardiac index and arterial–venous oxygen difference. This is produced by multiplying the y coordinates in (A) by cardiac index as given in (B). Oxygen consumption (a calculated variable) versus cardiac index is given in (C). A linear regression analysis of the mathematically coupled data in (C) is given.

variable. Figure 2 illustrates this type of mathematic coupling. The Y co-ordinate of Figure 2C is a calculated variable obtained by multiplying the Y and X variables of Figure 2A. In Figure 2A the data was obtained from random number tables. For discussion purposes, the X axis is arbitrarily called cardiac index and the Y axis called arterial–venous oxygen content difference. If one wishes to compare oxygen consumption with cardiac index then oxygen consumption, now a calculated variable, is obtained by multiplying arterial–venous difference times cardiac index. This is done by multiplying the X and Y variables of Figure 1A, given schematically as multiplying the Y co-ordinates of Figure 1A times the Y co-ordinates of Figure 1B, to produce Figure 1C. The two variables in Figure 1C appear to be statistically significantly related, the linear regression analysis correlation coefficient is 0.75, the standard error is small and the slope is significantly different from zero. This type of data and results are purely artificial, can be produced with random numbers and are due to algebraic coupling. Examples of this type mathematic coupling are Figure 3 of Siegel et al.[9], Figure 1 of Weisel et al.[10] and Figure 1 of Kennedy et al.[11]

A slightly more sophisticated, but just as common, technique of algebraic coupling is the inverse relationship of the Y and X variables produced by division coupling. Figure 3 illustrates this type coupling. In Figure 3A random numbers between 1 and 2 are given for the X variable which, for discussion purposes, is called oxygen consumption, and for the Y variable, which is called arterial–venous oxygen difference. If one wishes to compare arterial–venous oxygen difference to cardiac index then the later variable can be calculated by dividing oxygen consumption by cardiac index. The reciprocal of cardiac index is given in Figure 3B, and the result is given in Figure 3C. While the true mathematic relationship between the coupled variables arterial–venous difference and cardiac output is parabolic and not linear, there is sufficient variability that a linear regression is an acceptable approximation of the apparent functional relationship. Figure 3C suggests a strong inverse relationship between arterial–venous oxygen difference and cardiac index with a correlation coefficient of 0.77, a narrow standard error and a slope significantly different from zero. However, this result is entirely due to mathematic coupling and has no basis in reality, since

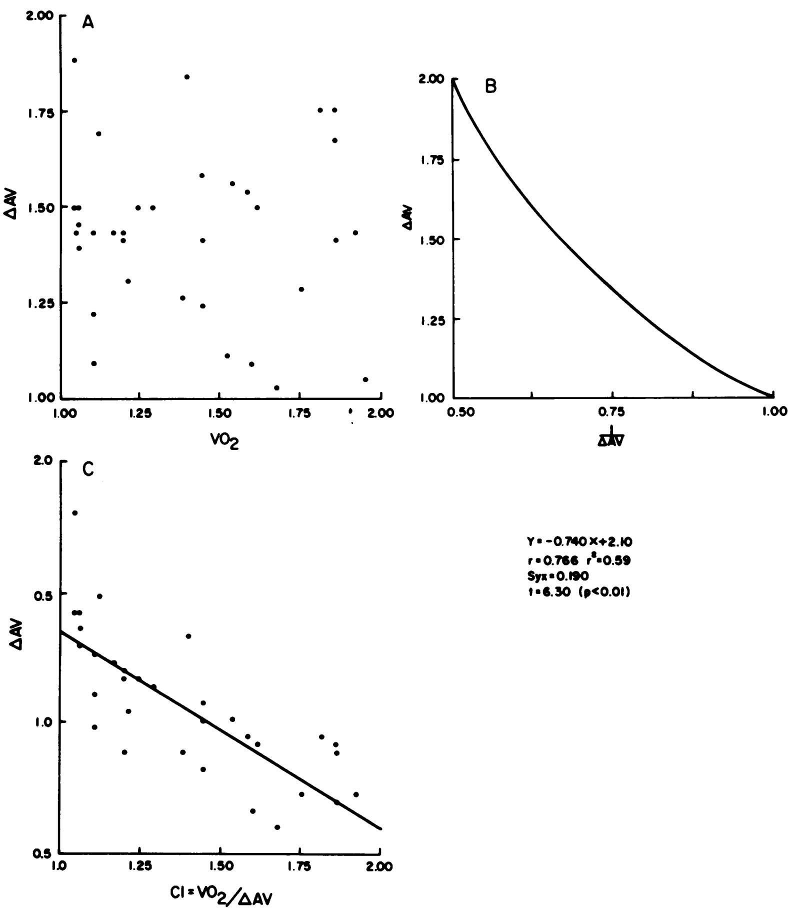

FIG. 3. Classical division coupling of variables. Arterial–venous oxygen content difference (Δ AV; Y axis) and oxygen consumption (VO_2, X axis) are the assumed measured variables given in (A), where the data was obtained from random number tables. Cardiac index (CI) is calculated by dividing oxygen consumption by the arterial–venous oxygen content difference. This is done by multiplying the Y axis of (A) by (B) to produce (C), arterial–venous oxygen content difference versus cardiac index. A linear regression analysis of the mathematically coupled data in (C) is given.

the data base were random numbers. A classical example of this type of coupled data has been published for laboratory animals in Figure 2 of Wright et al.[12] and for man in Figure 4 of Duff et al.[13] This data was interpreted to mean that there is a strong inverse relationship between arterial–venous oxygen content difference and cardiac index in septic shock.[12,13] In both of these studies[12,13] oxygen consumption, not cardiac index was the measured variable and cardiac index was calculated, as illustrated above. Comparison of calculated cardiac index to arterial–venous oxygen content difference produces coupled data identical to that of Figure 3C. Because of mathematic coupling, a correlation coefficient of 0.71 is expected ($r = 0.71$ then $r^2 = 0.50$, since 50% of the relationship between X and Y is due to coupling), and the authors[12,13] found correlation coefficients of 0.82 and 0.83, probably not significantly different from chance alone (0.71) when coupling is accounted for.

Vascular resistance is another hemodynamic variable that is frequently mathematically coupled, probably because it is a derived variable. For example, if systemic or pulmonary vascular resistance (resistance = pressure gradient/flow) is compared with pressure gradient then multiplication type coupling occurs (Fig. 2), and if resistance is compared to flow then division type coupling occurs (Fig. 3). Examples of mathematic coupling of vascular resistance with pressure or flow are given in Figure 5 of Kersten et al.[14] and Figure 1 of Siegel et al.[9] Other examples of division type algebraic coupling are given in Figure 3 of Daniel et al.,[15] Figure 2 of Berkowitz[16] and Figure 4 of Siegel et al.[9] Nonlinear division type coupling is illustrated by Figures 7–10 of Karayannacos et al.,[17] where the X axis is directly proportional to velocity and the Y axis is inversely proportional to the velocity squared.

Type 4 Mathematic Coupling

Physiologic coupling. As indicated above, mathematic coupling is possible when a calculated variable, such as vascular resistance, is compared with a measured variable, which is a component of the calculated variable, such as pressure gradient or cardiac output being compared with resistance. However, if two variables are not calculated, but are directly measured, it is still possible to have coupling between the two variables. This is called physiologic coupling. For example, if cardiac output and heart rate are directly measured and compared, it is expected that some linear relationship between the two variables will be found because cardiac output depends physiologically on heart rate. A recent article[18] illustrates the complexity of physiologic coupling in clinical investigation. In this study,[18] a significant relationship was found between the per cent increase in heart rate from control during nitroprusside infusion and the per cent change in systemic vascular resistance after nitroprusside withdrawal. Resistance was calculated from measured cardiac output and measured pressure gradient. Heart rate was measured independently and, therefore, there is no direct calculated algebraic coupling between resistance and heart rate. From the analysis of the relationship between change in heart rate from control (state 1) to nitroprusside (state 2) and change in resistance from nitroprusside (state 2) to final control (state 3), it is evident that the resulting apparent relationship between the changes in these two variables is due primarily to physiologic coupling, and is predictable from mathematic analysis. To analyze this relationship the subscripts 1, 2 and 3 are used to identify the two steps and three states, respectively—control, nitroprusside, and postnitroprusside, where HR is heart rate, SV is stroke volume, P is mean systolic pressure, CO is cardiac output ($CO = HR \cdot SV$), and R is resistance ($R = P/CO$). If Y is the fractional per cent change in heart rate from state 1 to state 2, then $Y = (HR_2/HR_1) - 1 = (HR_2/HR_3)(HR_3/HR_1) - 1$. If X is the fractional per cent change in R from state 2 to state 3, then $X = (R_3/R_2 - 1) = (P_3/P_2)(CO_2/CO_3) - 1$, or $X = (P_3/P_2)(SV_2/SV_3)(HR_2/HR_3) - 1$. Thus the equation of a line relating X and Y is $Y = a\ X + b$, where the slope a is $(P_2/P_3) \cdot (SV_3/SV_2) \cdot (HR_3/HR_1)$, and the intercept b is $b = a - 1$. The slope and intercept of the relationship between the X and Y variables depends on P_2/P_3, SV_3/SV_2 and HR_3/HR_1. They do not depend on P_1, HR_2, or SV_1. If one considers no change in heart rate between the initial and final state, $HR_3/HR_1 = 1$, and no change in pressure or stroke volume between the nitroprusside and final state, $(P_2/P_3) = (SV_3/SV_2) = 1$, then the equation $Y = a\ X + b$ predicts a slope of 1.0 and an intercept of 0. In Figure 4 of Packer et al.[18] the authors found a slope of 0.78 and an intercept of -0.22, not much different from what is expected if the only variable that changed was heart rate. The raw data of Figures 1–3 of Packer et al.[18] indicate that the calculated slope, a, is less than 1.0 because of the small relative directional changes in the measured variables determining the slope in the mathematic relationship. The intercept of the regression equation in Figure 4 of packer et al.[18] is −21.3%, or −0.213. If this value is substituted into the algebraic equation derived herein, a slope of 0.79 is calculated ($a = 1 - 0.21$) as compared with the regression equation slope of 0.78. This indicates that almost all of the apparent interdependence of changing heart rate during nitroprusside and per cent rebound change in systemic vascular resistance after stopping nitroprusside is due to physiologic coupling between the two variables. Only by comparing the raw data to the coupled relationship presented above can one determine that there is a significant difference in slope between the line predicted from the physiologic coupling and the actual measured data.

Physiologic coupling frequently occurs in dealing with the pulmonary shunt equation. For example, in Figure 1 of Berk et al.[16] the per cent change from control of the pulmonary shunt is compared with per cent change from control of cardiac output following an intervention. The shunt equation, $Q_s/Q_t = 0.0031\ (A - a\ DO_2)\ (Q_t/VO_2)$ where Q_s is the shunted blood flow and Q_t is the cardiac output, predicts that fractional per cent shunt (Q_s/Q_t) is directly related to cardiac output (Q_t) if one assumes that oxygen consumption (VO_2) is a constant, which it usually is unless cardiac output is very low. Accordingly, a linear relationship between calculated shunt and oxygen consumption is expected, as indicated herein Fig. 2 (type 3 coupling, multiplication). However, since cardiac output values were not used to calculate per cent shunt directly there is no direct algebraic coupling between per cent shunt and cardiac output, but there is physiologic coupling because of the linear dependence of shunt on cardiac output, when oxygen consumption is near constant.

A final example of physiologic coupling involves comparison of two variables, each of which is functionally dependent on a third variable. An example is given in Figures 2 and 3 of Sorensen and Enell[20] where peripheral and systemic vascular resistance changes are compared with changes in hematocrit. There is a physiologic relationship between peripheral vascular resistance and hematocrit. Since it is known that vascular resistance depends directly on blood viscosity, the higher the viscosity the higher the resistance, and since viscosity depends on hematocrit the higher the hematocrit the higher the viscosity. Thus, it is not surprising to find a relationship indicating that increases in peripheral vascular resistance are associated with increasing hematocrit and vice versa.[20]

This is an example of physiologic coupling and is predictable because of the known dependence of vascular resistance on viscosity and the dependence of viscosity on hematocrit.

Discussion

The four types of mathematic coupling presented herein, while they may be the more common types, are probably not the only types that occur in the surgical and medical literature. In each of the types presented statistical analysis plays a major role, but only in the final analysis of the data. The statistical methods are properly applied, but the error in data manipulation occurs earlier. The statistical analysis serves to support the apparent significant relationship between variables or changes in variables and, thus, tend to legitimatize the erroneous results and conclusions.

In many instances there may be some true functional relationship between two variables but, because of superimposed mathematic coupling, the functional relationship is overestimated. In the examples given in Figures 2 and 3 of this report the base data were obtained from random number tables and therefore the two "measured" variables should not have any true functional relationship to each other. Accordingly, the final erroneous but apparently significant results are due totally to mathematic coupling.

Analysis of Types 1, 2 and 3 mathematic coupling strongly suggest that when a variable is calculated from measured data and then compared with a second variable, the investigator should analyze the calculations to see if there is a dependent variable that is a component of both. If this is not the case, then any functional relationship between the two variables is probably real. On the other hand, if there is a common variable, then one must account for its effect on the relationship between the two variables.

In the illustration used of Type 1 mathematic coupling the statistical analysis played a major role in the erroneous results because the incorrect null hypothesis was assumed. This is evident only when the mathematical coupling is identified.

Type 2 mathematic coupling involves coupling between two calculated variables which have several common dependent variables which cancel out of the relationship between the two variables. The true relationship between the two variables is simpler and more easily predictable than expected. When calculated variables that have common components are analyzed for functional relationships, coupling is almost certain, and cancellation of some component variables is possible.

Type 3 mathematic coupling is by far the most common type and can be found throughout the literature. Algebraic coupling should always be suspected in the relationship between two variables when one or both are calculated. Algebraic coupling between two variables must be accounted for to obtain correct data analysis. Interpretations of the results should be formed with knowledge of the contribution of the pre-existing mathematic coupling.

Physiologic coupling, as described herein, is complex, interesting, and perhaps should be considered "soft" or indirect coupling." In the example presented the underlying common variable was change in heart rate, and while vascular resistance is not directly mathematically coupled to heart rate because heart rate was not used to compute resistance, there is indirect or physiologic coupling through heart rate. This guarantees a linear relationship between the two variables if change in heart rate varied over a reasonable range. Clearly, the possibility of physiologic coupling should be considered and accounted for when dealing with complex relationships between variables.

A general principle regarding mathematic coupling is to consider that it may play a role in any conclusions or statistical results relating calculated variables. If two or more variables are compared the effect of common component variables either through mathematic coupling, because one or more variables are calculated, or through physiologic coupling should be analyzed and accounted for.

Acknowledgments

The excellent technical assistance of Ms. Joy Powell is gratefully acknowledged.

References

1. Gore SM, Jones IG, Rytter EC. Misuse of statistical methods: Critical assessment of articles from BMJ from January to March, 1976. Br Med J 1977; 1:85–87.
2. Schor S, Karten I. Statistical evaluation of medical journal manuscripts. JAMA 1966; 195:145–150.
3. Rhodes GR, Newell JC, Shah D, et al. Increased oxygen consumption accompanying increased oxygen delivery with hypertonic mannitol in adult respiratory distress syndrome. Surgery 1978; 84:490–497.
4. Caruana JA, Gage AA. Increased uptake of insulin and glucagon by the liver as a signal for regeneration. Surg Gynecol Obstet 1980; 150:390–394.
5. Archie JP. Jugular venous pressure and carotid and jugular back pressure in patients undergoing carotid endarterectomy. Surg Forum 1977; 28:210–212.
6. Gale AW, Arciniegas E, Green EW, et al. Growth of the pulmonary anulus in pulmonary arteries after the Blalock-Taussig shunt. J Thorac Cardiovasc Surg 1979; 77:459–465.
7. Fuller TJ, Garg LC, Harty RF, et al. Severe hyperchlormic

acidosis complicating jejunoileal bypass. Surg Gynecol Obstet 1978; 146:567–571.

8. Scharf SM, Permutt S, Bromberger-Barnea B. Effects of hypoxic and Co hypoxia on isolated hearts. J Appl Physiol 1975; 39:752–758.
9. Siegel JH, Greenspan M, DelGuercio LRM. Abnormal vascular tone, defective oxygen transport and myocardial failure in human septic shock. Ann Surg 1967; 165:504–517.
10. Weisel RD, Dennis RC, Manny J, et al. Adverse effects of transfusion therapy during abdominal aortic aneurysectomy. Surgery 1978; 83:682–690.
11. Kennedy SK, Weintraub RM, Skillman JJ. Cardiorespiratory and sympathoadrenal responses during weaning from controlled ventilation. Surgery 1977; 82:233–240.
12. Wright CJ, Duff JH, McLean APH, MacLean LD. Regional capillary blood flow and oxygen uptake in septic shock. Surg Gynecol Obstet 1971; 132:637–644.
13. Duff JH, Groves AC, McLean APH, et al. Defective oxygen consumption in septic shock. Surg Gynecol Obstet 1969; 128:1051–1060.
14. Kersten TE, Mayer JE, Varco RL, Hemphrey EW. The nature of failure of pulmonary adaptation to atlectasis. Surgery 1977; 82:90–98.
15. Daniel AM, MacLean LD, Shizgal HM. Lactate metabolism in the dog during shock from hemorrhage, cardiac tamponade or endotoxin. Surg Gynecol Obstet 1976; 143:581–586.
16. Berkowitz HD. Diagnostic accuracy of oculopneumoplethysmography attachment for pulse volume recorder. Arch Surg 1980; 115:190–193.
17. Karayannacos PE, Talukder N, Nerem RM, et al. The role of multiple noncritical arterial stenoses in the pathogenesis of ischemia. J Thorac Cardiovasc Surg 1977; 73:458–469.
18. Packer M, Meller J, Medina N, et al. Rebound hemodynamic events after the abrupt withdrawal of nitroprusside in patients with severe chronic heart failure. N Engl J Med 1979; 301:1193–1197.
19. Berk JL, Hagen JF, Tong RK, et al. The role of adrenergic stimulation in the pathogenesis of pulmonary insufficiency. Surgery 1977; 82:366–372.
20. Sorensen MB, Enell HC. Blood volume and hemodynamic changes in relation to extensive vascular operations. Surg Gynecol Obstet 1978; 147:369–375.