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Boolean Algebra for Laboratory Diagnostics in Medicine

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Abstract

Background: Medical diagnostic tools have become increasingly complex in the last decade. Numerous permutations are necessary to come to the correct decision on how to treat a patient.

Aim: This study used Boolean algebra to define laboratory parameters by disease entity. We assigned each parameter to a group of disease entities. Since we did not want to give the impression that the respective list of diseases strictly determined the laboratory parameters, we used the mathematical symbol ≈ for approximation in the equations.

Results: A system of linear Boolean equations permitted assignment of each laboratory parameter to a set of disease entities. Addition of the linear equations by use of the axioms of Boolean algebra resulted in assignment of a disease entities to laboratory parameters.

Conclusion: Linear Boolean equations may have the potential to become part of diagnostics in medicine.

Keywords: boolean algebra; linear equations; medicine; diagnostics

Introduction

Precision medicine is a crucial condition for patient-tailored treatment decisions. It enables exact definition of disease and risk-stratified treatment guidelines. This is especially important for life-threatening diseases, such as myocardial infarction or acute leukemia, which require swift action. The international statistical classification of diseases and related health problems (ICD) from the World Health Organization (WHO) has been beneficial in developing a standardized approach to disease management; the latest version is ID 11 (Cazzola and Sehn 2022). In addition to the classical approach of anamnesis and physical examination, numerous technical tools have become available for decision-making on treating patients (Swerdlow et al. 2008, 2017, Alaggio 2022, Cazzola and Sehn 2022). Boolean algebra is useful for the definition of hematologic malignancies In this study, we have developed a system of linear Boolean equations to (Zugmaier et al. 2019, 2021, 2023) enable assignment of laboratory parameters to disease entities and vice versa.

Materials and Methods

The binary system, including 2 integers, is used. It can be easily transferred from the decimal system (Hoffmann 2016):

0=0, 1=1, 2=10, 3=11, 4=100, etc.

The following axioms are used as defined by Shannon (1940)

- The rules of arithmetic for addition and multiplication apply.
- The symbols of addition multiplication and equations are worldwide accepted and known; therefore, they are not explained in the list of abbreviations and symbols.
- The result of an addition or multiplication can only be 1 or 0. No other numbers are permitted.
- Addition:
  - 1 + 1 +1 …+ 1 = 1
  - 1 + 0 + 0…+ 0 = 1
  - 0 + 1 + 1…+ 1 = 1
  - 0 + 0 + 0 …+ 0 = 0
  - 1 + 0 = 0 …+ 1
- Multiplication
  - 1 x 1 x 1….x 1 = 1
  - 1 x 0 x 0 …x 0 = 0
  - 0 x 1 x 1 …x 1 = 0
  - 0 x 0 x 0….x 0 = 0
  - 1 x 0 = 0 x 1
- instead of = for "equal" ≈ for "approximately" equal is used, for reasons of practicality we still use the term "equation" Instead of the term "approximation"

Abbreviations and Symbols

AA aplastic anemia

ACE angiotensin converting enzyme

ACTH adrenocorticotropic hormone

AG anion gap

ALL acute lymphocytic leukemia ALT alanine aminotransferase

AML acute myeloid leukemia

AP alkaline phosphatase

Approximate ≈

AST aspartate aminotransferase

Ca^{2+} calcium

Cl^- chloride

CLL chronic lymphocytic leukemia

CML chronic myeloid leukemia

Decreased ↓

Ig immune globulin

Increased ↑

K^+ Potassium
LDH lactate dehydrogenase

MDS myelodysplastic syndrome

Mg^{2+} magnesium

MM multiple myeloma

Na^+ Sodium

NHL non-Hodgkin lymphoma

PV polycythemia vera

RA rheumatoid arthritis

SIDADH syndrome of inappropriate antidiuretic hormone secretion

SLE systemic lupus erythematosus

Results

AP↑ ≈ hyperparathyroidism + acromegaly + hyperthyroidism + Paget + hepatitis + sarcoidosis + cholestasis + mononucleosis + osteomyelitis + malignant bone tumor + metastasis osteomalacia + albumin injection + vitamin B12↓ ↓ + phosphate↑ + weight↓ + dehydration + infarction + osteomyelitis + cirrhosis + chlorpropamide + ergosterol +

AP↓ ≈ hypothyroidism + osteoporosis + celiac disease + vitamin D↑+ vitamin C↓+ milk – alkali syndrome + vitamin B12↓

$AG = Na^+ - (Cl^- + HCO_3^-)$

AG↑≈ ketoacidosis + salicylates + methanol + ethylene glycol + propylene glycol + lactic acidosis + renal failure

AG↓ ≈ MM + lithium

ALT↑ ≈ hepatitis + mononucleosis + liver abscess + cholestasis + alcohol + malignant tumor

AST↑ ≈ diabetes mellitus + muscular dystrophy + Paget + cholecystits + hepatitis + pneumonia + hemolysis + polymyositis + pancreatitis + ileitis + exercise + tonic and clonic seizures + rhabdomyolysis + peptic ulcer + uremia + vitamin B12↓ + myoglobulinemia + salicylates + alcohol + dehydration + malignant tumor + infarction + ulcerative colitis + muscle necrosis + intramuscular injections + hepatic necrosis + cholestasis + uremia

Bicarbonate↑ ≈ aldosterone↑ + Cushing + hypothyroidism + metabolic alkalosis

Bicarbonate↓ ≈ Addison + ventilation↑ + metabolic acidosis

Ca^{2+}↑ ≈ hyperparathyroidism + hyperthyroidism + hypothyroidism + Cushing + Addison + osteoporosis + Paget + sarcoidosis + immobilization + vitamin D↑ + milk-alkali syndrome + thiazide diuretics + berylliosis + malignant tumor

Ca^{2+}↓ ≈ hypoparathyroidism + pregnancy + pancreatitis + renal insufficiency + fluids↑ + malabsorption + corticosteroids + vitamin D↓+ corticosteroids

CL↑ ≈ hyperparathyroidism + diabetes mellitus + diabetes insipidus + respiratory alkalosis + metabolic acidosis

Cl^- ↓ ≈ ketoacidosis + Addison + aldosterone↑ + cardiac failure + pyloric obstruction + metabolic acidosis + metabolic alkalosis + emphysema + diuretics

LDH↑ ≈ muscle disease + hypothyroidism + hepatitis + mononucleosis + hemolysis + cholestasis + intestinal obstruction + celiac disease + vitamin B12↓ + folic acid↓ + alcohol + NHL + Hodgkin + ALL + AML + CLL + CML + infarction + polymyositis + dermatomyositis + muscle necrosis

Phosphate↑ ≈ Fanconi + acromegaly + hyperparathyroidism + Paget + sepsis + sarcoidosis + fracture + intestinal obstruction + renal failure + vitamin D↓ + muscle necrosis + milk – alkali syndrome + respiratory alkalosis + vitamin D↑ + MM + osteolysis + AML + CML

Phosphate↓ ≈ hypoparathyroidism + diabetes mellitus + Fanconi + vitamin D↓ + diarrhea + vomiting + gout + ketoacidosis + respiratory alkalosis + K^+↓ + Mg^{2+}↓ + androgens + epinephrine + glucagon + insulin + salicylates + antacids + alcohol + intravenous glucose + anabolic steroids

K^+↑ ≈ aldosterone↓ + Addison + rhabdomyolysis + hemolysis + urinary obstruction + renal failure + acidosis + muscle necrosis + amiloride + spironolacatone + triamterene + ACE inhibitors + food + status epilepticus + hemorrhage + fruit juice + soft drinks + oranges + peaches + bananas + tomatoes + protein diet↑

K^+↓ ≈ diabetes mellitus + Cushing + aldosterone↑ + ileus + vomiting + metabolic acidosis + pyelonephritis + diuretics + estrogens + salicylates + corticosteroids + aldosteronoma + villous adenoma + colonic cancer + Zollinger-Ellison syndrome + metabolic alkalosis

Albumin↓ ≈ an albuminemia + diabetes mellitus + hepatitis + ulcerative colitis + protein - losing enteropathy + glomerulonephritis + SLE + polyarteritis + RA + rheumatic fever + peptic ulcer + congestive heart failure + cirrhosis + nephrotic syndrome + estrogens + MM + Hodgkin + ALL + CLL + macroglobulinemia

IgG↑ ≈ tuberculosis + hepatitis + osteomyelitis + SLE + RA + vasculitis + vasculitis + cirrhosis + MM

IgG↓ ≈ agammaglobulinemia + lymphoid aplasia + common variable immune deficiency + nephrotic syndrome + MM + CLL

IgA↑ ≈ Wiscott Aldrich + SLE + RA + sarcoidosis + cirrhosis + MM

IgA↓ ≈ absent in 3 per 100,000 + hereditary telangiectasia + lymphoid aplasia + nephrotic syndrome + Still + SLE + common variable immune deficiency + agammaglobulinemia + cirrhosis + ALL AML + CLL + CML

Na^+↑ ≈ diabetes insipidus + diabetes mellitus + hyperparathyroidism + aldosterone↑ + corticosteroids + diuretics + thalamic lesion

Na^+↓ ≈ Addison + pneumonia + brain abscess + SIADH + congestive heart failure + cirrhosis + lung cancer + meningitis

Pancytopenia ≈ AA + PNH + tuberculosis + hepatitis + SLE + irradiation + vitamin B12↓ + folate↓+ chemotherapy + benzene + MM + MDS + AML + ALL + myelofibrosis + Hodgkin + non-Hodgkin

Reticulocytes↑ ≈ hemorrhage + hemolysis + response to treatment

Reticulocytes↓ ≈ deprivation + anemia of chronic disease + bone marrow failure + Fe↓ + vitamin B12↓ + folate↓

Uric acid ↑ ≈ polycystic kidney + sickle cell anemia + Wilson + Fanconi + von Gierke + Down + Indians + Filipinos + Maoris + hypothyroidism + hypoparathyroidism + hyperparathyroidism + psoriasis + hemolysis + sarcoidosis + renal failure + diuretic + salicylate + lead + berylliosis + hypertension + metabolic syndrome + ALL + AML + CLL + CML + MM + PV + NHL + Hodgkin

Uric acid↓ ≈ xanthinuria + Fanconi + Wilson + Dalmatian dog mutation + acromegaly + celiac disease + allopurinol + ACTH + contrast media + carcinoma + Hodgkin

Diseases can easily be assigned to laboratory parameters. The laboratory parameters of each row, in which the disease entity is listed, are added. This is shown here by using SLE as example.

SLE ≈ albumin↓ + IgA↓ + IgA↑ + pancytopenia. This example shows an increased as well as a decreased IgA level can point to an SLE.

Discussion:

Boolean algebra is a mathematical basis of computer science. It uses a binary system restricted to the integers 0 and 1. Permutations of various inputs of binary numbers can only result in an output of either 1 or 0, not both. Any other integer is not permitted. The gates in computer science are defined by the mathematical operators of Boolean algebra. In this study we used the AND gate and the OR gate. The AND gate is identical to multiplication. The OR gate is identical to addition with one exception, 1 + 1 =1 (Shannon 1940). In regular binary arithmetic 1 + 1 = 10 would account. This is not possible in Boolean arithmetic, since it can have only 1 or 0 as result of computations. This approach has the advantage of simplifying arithmetic operations and enabling the calculation of complex permutations. Since the equations do not claim a strict relation, the mathematical symbol ≈ for approximation has been used.

In this study, we used linear Boolean equations to standardize the relationship between laboratory parameters and disease entities. Linear equations in Boolean algebra have been investigated over decades (Melter and Rudeanu 1984). To our knowledge, this system of linear Boolean algebra study is used for the first time in medicine and has never been applied before.

Mathematics in medicine. Become a crucial component of all exact sciences, including medicine, physics, and chemistry. Clinical research would not be possible without biostatistics and mathematical modeling (Matthäus and Matthäus 2020).

Boolean algebra has successfully been used in various areas of medicine. This application includes laboratory and clinical research (Albert and Robeva 2015, He et al. 2015, Lin and Khatri 2014, Macauley and Young 2020, Varadan and Anastassiou 2005, DiAndreth 2022, Riede et al. 2008, Palma et al. 2021, Zugmaier and Locatelli 2019, 2021 and 2022).

The term "mathematical logic" sometimes used instead of "Boolean algebra" is misleading and should be abandoned. Logic is crucial for any rational endeavor also for mathematics, but logic is not a mathematical subdiscipline (Grattan-Guiness, 2000).

The definition of logic as part of mathematics leads to circular statements. Misleading notions such as "truth values" should be avoided. We have used numbers as done in arithmetic operations (Steffens et al. 2020). Our approach is purely mathematical.

The mathematical symbols in new mathematical areas are difficult to understand since they lack standardization and standardization is often not accepted, by part of the mathematical community (Vivaldi 2014). This is especially true for Boolean algebra. There is no consensus on the symbols to be used, resulting in the use of different symbols for the same mathematical operations (Hoffman 2016). On the other hand, the same symbols are used for various mathematical operations. In this study we have only used symbols of ordinary arithmetic and algebra, which have been accepted and used worldwide.

This study has limitations. The linear equations can provoke an unjustified impression of certainty, which can rarely be achieved in medicine. The linear equations used in this study are rather approximations and not equations in the strict sense (see Materials and Methods). The physician will always have the last word on how to apply such a system. This holds true for any tool of diagnostics in medicine.

In conclusion, linear Boolean equations have been shown to be a useful part of diagnostics in medicine. This is the first application of linear Boolean equations in medicine.

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