Chapter 6

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Computer Diagnosis of Congenital Heart Disease

During the past two decades electronic computers have come into increasingly active use and are now regarded as essential in the daily function of business, industry, and science. Much the same as machines during the industrial revolution extended man's ability to perform more difficult and exacting tasks of physical labor, modern electronic computers are now extending man's ability to perform more difficult and exacting tasks of mental labor. Although this unique machine can process great masses of data at electronic speeds, it functions only under man's direction, and like any other tool or machine is dependent upon the skill and experience of the person who directs it. In the field of medicine there are few men who can direct or "program" a computer to solve a given problem. Accordingly, the use of computers in medicine has been somewhat limited. When doctors become more familiar with the function of computers they will begin to work more freely with programmers, who are specially trained to direct or "teach" the computer how to solve a particular problem. The programmer must direct the computer, but it will be necessary for the doctor to supply the necessary data.

Significant contributions have already been made with the application of computers as an aid to diagnosis in cardiology, particularly in electrocardiography[9, 10] and phonocardiography.[2, 3] This chapter will deal primarily with two computer programs developed in the Cardiovascular Laboratory of the Latter-day Saints Hospital, Salt Lake City, Utah, for the diagnosis of congenital heart disease. In one program the clinical diagnosis is made by computer solution of a probability equation which utilizes statistical data consisting of the incidence of specific findings in specific disorders. In the other program the catheterization diagnosis is established from computer processing of data derived directly from electrical transducers (oximeter and strain gage) during the cardiac catheterization.

Clinical Diagnosis

On first thought the clinician quite naturally might doubt that the art of diagnosis with its many subtleties could be adapted to a mathematical expression capable of being solved by a computer. However, in discussions with the patient or his parents he often says, "I am practically 100% certain," or, "there is a fifty-fifty probability." This was well appreciated by Sir William Osler at the turn of the century when he said, "Medicine is a science of uncertainty and an art of probability."[8] If the computer could serve in predicting probability, its role as a contributor in medical diagnosis would not be so remote.

The possibility that a computer could be utilized in this way was first considered in our laboratory in 1960. The basis came from a report by Ledley and Lusted, who suggested the possible relationship of Bayes' theorem to the logical process used in medical diagnosis.[6] The following equation was originally stated by Bayes in 1763 as a theorem of inverse probabilities:

$$P\left(\frac{yi}{xj}\right) = \frac{P(yi)\ P(xj/yi)}{\sum_{\text{all } k} P(yk)\ P(xj/yk)}$$

In the expression of this theorem, the term $P(yi/xj)$ represents the probability that a patient with ith disease (yi) will present with the jth symptom complex (xj). $P(yi)$ represents the incidence of the disease in the population under consideration. $P(xj/yi)$ is the term representing the incidence of the jth symptom in the ith disease. The subscript k in the denominator represents each disease in sequence. $\sum_{\text{all } k}$ represents the summation or total incidence of jth symptom in the population under consideration.

The following equation is a modification of Bayes' theorem and was derived in the authors' orginal article on this subject[14]:

$$P_{y_1/(x_1,x_2,\cdots,x_j)} = \frac{P_{y_1}\ P_{x_1/y_1} \cdots P_{x_j/y_1}}{\sum_{\text{all } k} P_{y_k}\ P_{x_1/y_k}\ P_{x_2/y_k} \cdots P_{x_j/y_k}} \qquad (1)$$

The terms in this equation are defined as follows:

P = probability. The computer program is so compiled that this is given in the nearest percent, i.e., 0.01 or 1%, and 0.99 or 99% probability.

y_1 = disease 1. We have considered 33 different disease entities and thus the list would extend from y_1 to $y_2 \ldots y_{33}$.

x_1 = symptom 1. The word "symptom" is used inclusively for *all* findings, not only from history but all those encountered on physical examination, phonocardiogram, electrocardiogram, and the roentgenogram. We have selected a total of 57 such symptoms. Equation (1), although appearing formidable, states simply that the probability of disease y_1 existing in a patient who presents a particular set of symptoms represented as $x_1, \cdots, x_j$ can be calculated if the following facts are known:

1). P_{y1}, the probability or incidence of disease y_1 occurring in the disease group under consideration. This population subgroup consists of all the patients referred to the cardiovascular laboratory with the diagnosis of congenital heart disease.

2). The probability of symptom x_1 occurring in disease y_1, x_2 occurring in y_1, and so forth for each symptom.

3). The incidence figure for each symptom must be known for each disease.

The search for the informational data as well as the tedious multiplication and division necessary to solve this equation can be done on a practical basis only by a computer.

The probability or incidence figures for given symptoms occurring in given types of congenital heart malformations is information that should be easy to compile. We sought such figures in standard texts,[5,7,12] which were of great help, but we were disappointed in other sources in the literature. Sufficient information was frequently either not given or was not compatible with our own experience. Thus the symptom-disease coincidence figures for the most part represent what we considered logical and consistent with our experience and understanding of the basic pathologic physiology of the disorder. These figures were compiled into a probability table, or symptom-disease matrix, with a total of 57 symptoms along the x axis and a total of 33 diseases along the y axis. The 1,914 coincidence figures in this matrix have been stored on punched cards and on a magnetic disc pack for computer use.

Certain assumptions concerning the matrix figures and the equation must be made. First, the symptoms are assumed to be independent of one another within a given disease. Second, the diseases themselves are assumed to be mutually exclusive. For example, if a patient has a combination of defects, the combination must be considered a new disease and the symptom-disease matrix has to be expanded to include it. To illustrate, consider the two diagnoses pulmonary stenosis and atrial septal defect. Alone, neither would produce cyanosis. It would, therefore, be impossible to predict the combination of these lesions if cyanosis were present. Thus the combination of pulmonary stenosis and atrial septal defect must be considered a new disease entity.

Our original matrix has required frequent updating in an attempt to improve the accuracy of the probability of symptoms as we have accumulated more accurate data. The incidence of each disease is directly related to the type of patient referred to the laboratory and, therefore, will change from time to time. For example, our initial incidence figure for atrial septal defect was 0.081, but following review of our first 637 cases the incidence was found to be 0.160. Similarly, aortic stenosis was changed from 0.045 to 0.095. It should further be stated that the matrix figures reflecting the population experience in our laboratory could be quite different for another laboratory, particularly if the laboratory should deal with a specific age group.

Diseases

The first disease listed in the matrix is termed "normal." In approximately 15% of the cases referred to our laboratory with the diagnosis of congenital heart disease no significant hemodynamic abnormality can be demonstrated. We have found that some of these individuals fit a rather well-defined clinical picture in which a "functional" systolic ejection murmur is accompanied by a qR pattern in lead V1 on the electrocardiogram and the pulmonary artery appears prominent on the chest film. We have considered reclassifying these patients into a separate disease group because their findings fit the clinical picture of "straight-back syndrome."[11]

There are 33 disease entities in our list. The list is obviously incomplete and does not include corrected transposition of the great vessels, infradiaphragmatic pulmonary venous connection, anomalous systemic venous return, hypoplastic left heart syndrome, dextrocardia, etc. Our list now is actually smaller than it was initially, since some lesions with essentially the same manifestations were listed as separate entities. This was true for atrial septal defect and partial anomalous pulmonary venous connection. Because of its much greater frequency and because the two are frequently seen as combined lesions, we now list only atrial septal defect, with or without partial anomalous pulmonary venous connection.

We have listed as separate disease entities congenital heart defects which have the same type of anatomic defect but have variable manifestations because of factors such as size or severity of the defect and pressure relationships between systemic and pulmonary circulations. For example, isolated ventricular septal defects were divided into three separate entities: those with small left to right shunts, those with moderate to large left to right shunts, and those with "pulmonary hypertension" (pulmonary vascular occlusive disease). The division between "small" and "large" left to right shunts was arbitrarily set at a level where pulmonary flow to systemic flow ratio was 1.4, with the patient at rest breathing room air. Pulmonary hypertension was arbitrarily defined as being equal to or exceeding systemic pressure. The presence of pulmonary hypertension would thereby modify not only the manifestations of a ventricular septal defect but also atrial septal

defect and patent ductus arteriosus. These combinations also have to be listed as separate disorders. Similarly, the manifestations of pulmonary stenosis will vary with the severity of the gradient. Here an arbitrary figure of 40 mm Hg was decided upon to differentiate the "mild" pulmonary stenosis from the "severe." While these subdivisions of the same anatomical defect were based upon our ability to divide them by their clinical manifestations, the divisions had some practical value, in that such a classification tended to place a patient in an operable or nonoperable category. In the case of ventricular septal defects, those with the small shunts and those with pulmonary vascular occlusive disease (pulmonary hypertension) would not be surgical candidates, leaving only those with significant left to right shunts for surgical consideration.

Symptoms and Checkoff List

The 57 symptoms to be considered by the computer program were recorded as a checkoff list. The first symptom category contains the age of the patient. This is a valuable differentiating symptom because the age of the patient at the time of his referral to the laboratory makes some diagnoses considerably more likely than others. For example, an uncomplicated atrial septal defect is not likely to be studied under 1 year of age, whereas such lesions as pulmonary atresia and transposition of the great vessels are practically always evaluated in a cardiovascular laboratory before 1 year of age.

Four of our listed symptoms deal with the types and degree of cyanosis that might be encountered. If there is to be any differentiating component in this category, then no more than one form of cyanosis can be considered. The same could be stated for murmurs, because a holosystolic and a midsystolic murmur could not be simultaneously present in the same area. If more than one symptom in a bracketed group (indicates that symptoms are mutually exclusive and only one of the group can be considered by the computer program) is considered by the observer completing the checkoff list, the computer will not attempt a diagnosis and will print out "symptom error."

The clinician relies heavily upon auscultation as an aid in differentiating types of congenital heart disease. From the checkoff list of symptoms it is apparent that this approach relies heavily on the importance of murmurs as factors in differentiation. All patients evaluated in this program have had phonocardiograms as well as clinical auscultation. The checkoff list is so designed that the murmur can be defined by the following characteristics:

1. Site of maximum intensity
2. Time (systolic and diastolic)
3. Time course of intensity
   a. Systolic
      (1) Holosystolic (regurgitant)
      (2) Midsystolic (ejection)
   b. Diastolic
      (1) From atrioventricular valves
         (a) Early (ventricular filling)
         (b) Late (atrial emptying)
      (2) From semilunar valves
         (a) Holodiastolic
         (b) Diastolic only
   c. Continuous
4. Intensity

More than one site can be considered if the site of maximum intensity cannot be determined with confidence. The phonocardiogram is nearly as helpful in this regard as it is in defining the time course of intensity of the murmur. Even with a phonocardiogram, a murmur may occasionally be difficult to put into a subclassification. When a systolic murmur, for example, cannot with confidence be considered either midsystolic or holosystolic, only the undifferentiated systolic murmur is considered. Although this results in some loss of differentiation, it allows the physician to supply the computer with information which is more accurate in this situation.

Some lesions, such as aortic stenosis, give rise to loud murmurs, while others, such as an atrial septal defect, produce murmurs that are softer. Thus the intensity of the murmur can be a valuable differentiating feature. Grade 3/6 murmur was arbitrarily chosen by the authors as the division between "soft" and "loud" murmurs. From the phonocardiogram (recorded by an Elema Schonander Model 21C phonocardiograph) a murmur that causes a 10-mm deflection at 1/5 sensitivity is considered to be greater than grade 3/6 intensity (symptom 31).

The intensity of the second sound, specifically the pulmonary component, is a cardinal point of focus for the cardiologist, since this is the auscultatory means of distinguishing pulmonary hypertension, normotension, or hypotension. Wide splitting of the second sound without respiratory variation (fixed split) is a time-honored clinical finding differentiating an atrial septal defect from other causes of left to right shunting. Other auscultatory findings, such as ejection clicks and third and fourth heart sounds, were not listed, because we felt that these findings did not supply sufficient differential information to be included in the checkoff list.

Electrocardiographic criteria have been kept relatively simple, so differentiation is primarily by definition of right or left ventricular hypertrophy. Axis deviation, although not totally reliable as an indication for ventricular hypertrophy, is valuable in differentiation of endocardial cushion defects. T-wave inversion in lead V6, in our former checkoff lists, had the qualifying instruction, "in absence of digitalis." This qualification is still required for this symptom. This symptom is, of course, extremely valuable as a differentiating factor for primary myocardial disease in the younger patient and for left ventricular hypertrophy in the older child and adult.

The x-ray data are derived from review of a single

6-foot chest film. This, admittedly, limits the amount of x-ray information we can provide the computer program, but most of the x-ray information utilized in this diagnostic program can be found on a single chest film and the symptoms are rather easy to define. There are two symptoms, rib-notching, and "snowman," which have great differentiating power, since they are limited to coarctation of the aorta and to supradiaphragmatic total anomalous pulmonary venous connection, respectively. The bulk of the x-ray data are so arranged that the status of the pulmonary circulation is defined by description of the peripheral and hilar vessels and the pulmonary artery trunk.

We initially had a set of complaints offered by the patient as a symptom group. This included squatting, dyspnea, easy fatigue, orthopnea, chest pain, frequent respiratory infections, and syncope. With the exception of squatting, these complaints were difficult to evaluate and were found to contribute little to differentiation of one lesion from another and, accordingly, are no longer used. There has been a distinct trend to simplify all criteria and to rely on fewer symptoms. A symptom offers the greatest contribution when it (1) has a high power of differentiation and (2) can be accurately observed. At the present time we are eliminating four symptoms, forceful apical thrust, opening snap or accentuated M_1, right ventricular hyperactivity, and pulsatile liver from the computation to determine if their indication of right or left ventricular hypertrophy or of mitral or tricuspid valve disease can be more reliably demonstrated by other symptoms available on the checkoff list. It should be stressed that even though this diagnosis program has been in operation for nearly 6 years, this should not be considered to be a finished product, because it is evident that changes must frequently be made as new data and experience are gained.

Mechanics of Computer Diagnosis

The mechanics involved in the flow of information to a computer diagnosis is illustrated in Fig. 6.1. The physician, after evaluating the patient and reviewing his phonocardiogram, electrocardiogram, and chest x-ray, marks the symptoms on the checkoff list. On the back side of the checkoff list he records his differential diagnosis and gives a probability rating to each diagnosis. This allows a comparison to be made between physician and computer diagnosis with the follow-up diagnosis. The checkoff list is then given to the laboratory secretary, who punches the appropriate code numbers on punch cards. The computer has previously been prepared by being "fed" the information from the symptom-disease matrix and the program instructions. This information can be supplied by reading in coded punched cards or, as is generally the case, the information is more readily provided by magnetic tape or data disc pack. The patient's symptom card is then "fed" to the computer and the computation is completed. The print-out includes a listing of the symptoms checked, followed by all diagnoses considered by the computer. Each of the diagnoses in the listing is followed by the percent probability given by the computer as calculated from the modified Bayes' theorem. The diagnosis given the highest probability is listed first and is followed by all other diagnoses in decreasing order of probability, including only those with 1% or greater probability.

Program Evolution

Equation (1) considers only those symptoms present in the patient. The absence of symptoms can also be equally contributory; e.g., absence of a systolic murmur along the upper left sternal edge rules out pulmonary stenosis. Because absence of information is also utilized in the consideration of a diagnosis, Eq. (1) has been modified as follows:

$$P_{y_j/(a_1,a_2,\cdots,a_n)} = \frac{P_{y_j}\prod_{i=1}^{i=n}(P_{x_i/y_j})^{a_i}(1-P_{x_i/y_j})^{1-a_i}}{\sum_{j=1}^{j=k}(\text{numerator})_j} \qquad (2)$$

The new terms introduced into this equation are:

1. a, which can have two values; i.e., $a = 1$ if the symptom is *present*, $a = 0$ if the symptom is *absent*.
2. $\prod_{i=1}^{i=n}$ is the term designating the product of the terms in the numerator.

If the ith symptom (x_i) is *not* present, the calculation for the probability of the jth disease (d_j) can employ only the complement of the incidence figure for symptom x_i occurring in disease y_j, since a_i is equal to zero. This modification allows the equation to consider the absence of a symptom as positive information. Although this represents a more complicated equa-

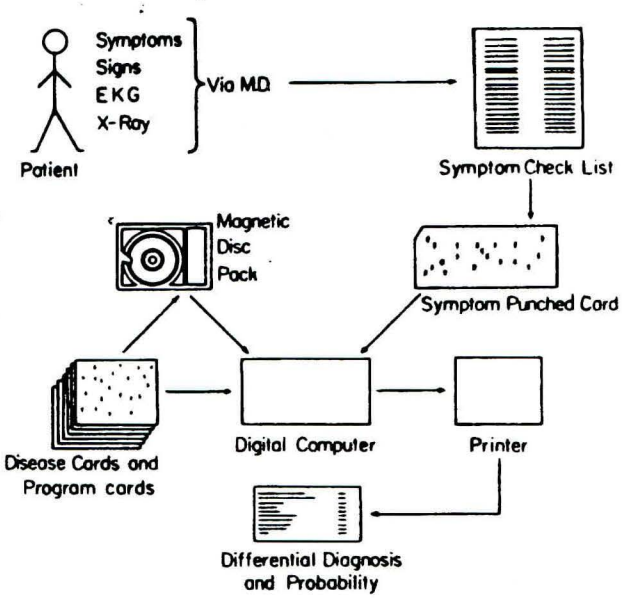

FIG. 6.1. Informational flow from the patient through computer processing to a diagnosis.

tion, it is not of significance as far as computer solution is concerned. It, too, does not require an addition to the symptom-disease matrix. The computer performance has been so improved by the use of Eq. (2) that it now equals the performance of experienced cardiologists (see Fig. 6.2).

In both Eqs. (1) and (2), the computer regards the symptoms as either 100% present or 100% absent. In clinical medicine, however, it is difficult for the examining physician to be so totally objective, and he may well be uncertain about any given finding, e.g., whether the second sound is fixed in its split. To accommodate this, the computer program has been further modified so that the doctor, in completing his checkoff list, may weight the symptom about which he is uncertain by grading it. If the doctor is totally uncertain as to its presence or absence, he marks the symptom 0.5, indicating that he considers it is equally probable that the symptom is present or absent. This symptom is then eliminated from consideration in the equation. If he feels the symptom is probably present, he can give it a rating of 0.6 to 1.0, depending on how certain he is. If he feels the symptom is absent but is not fully confident, he can rate the symptom from 0.1 to 0.4.

The weighting of symptoms has required further modification of the probability equation:

$$P_{w_j/(a_1,a_2,\cdots,a_n)} = \frac{P_{w_j}\prod_{a=1}^{a=n}\left[a_i(P_{s_i/w_j}) + (1-a_i)(1-P_{s_i/w_j})\right]}{\sum_{j=1}^{j=k}(\text{numerator})_j} \quad (3)$$

No new terms are introduced by this equation, but a can now be any value from 0.0 to 1.0. This gives the doctor some latitude in evaluating the severity of a symptom. Although this equation is more complicated, it is insignificant as far as computer solution is concerned and it does not require any alteration of the matrix. When Eq. (3) is used, the probability figure for the correct diagnosis is understandably lower. However, more diagnoses are listed in the differential diagnosis, reflecting the uncertainty of the physician in his consideration of some symptoms.

Program Evaluation

A follow-up diagnosis has been established in each case by cardiac catheterization. This has frequently been confirmed by surgical or postmortem visualization. The follow-up diagnosis has provided a reference by which the physician's and the computer's diagnosis can be compared. The comparison enables us to test the logic of the computer program but not the accuracy of the observations, since both the computer and the physician are utilizing the same set of observations. Our initial experience confirmed the logic of the program. We found that the correct diagnosis with the highest probability was made by the computer more consistently when supplied with information from the more experienced observer (Fig. 6.3). In this diagram J. S. is a second-year resident in internal medicine, A.F.T. is a cardiovascular physiologist, and L.G.V. is a pediatric cardiologist with the most clinical experience of the three observers. The less experienced observer (J. S.), in addition to making the correct diagnosis less frequently, also tended to make less accurate observations, and the computer's performance accordingly fell when supplied with data from his checkoff lists. As more experience has been gained with the program, the performances of A.F.T. and L.G.V. have improved. The performance of the computer also improved, even more strikingly. This improvement can be attributed to three factors: (1) the computer is now being provided with more accurate observational data from the physician observers, (2) the symptom-disease matrix has been continually improved as additional statistical experience has been gained, and (3) the probability equation has been modified to allow inclusion of absence of symptoms as positive information.

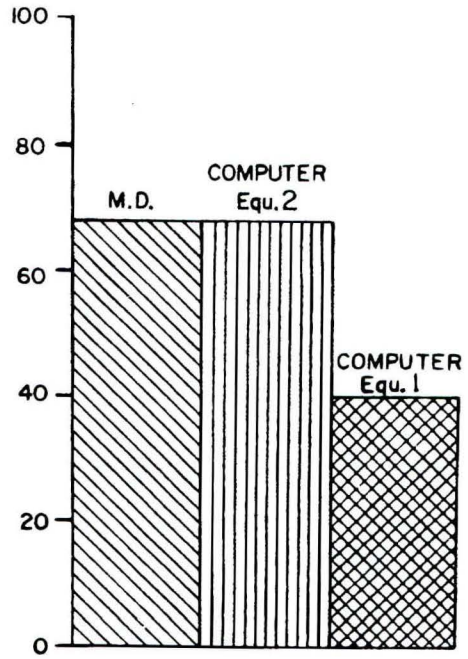

FIG. 6.2. Comparison of the probability rating given the correct diagnosis by the computer using Eqs. (1) and (2) with the physician's rating. Note the improved performance of the computer when the probability equation utilizes absence of symptoms as positive information (From Toronto, A. F., Veasy, L. G., and Warner, H. R. Evaluation of a computer program for diagnosis of congential heart disease. *Progr. Cardiov. Dis.*, 5: 362, 1963. Reprinted by permission.)

To test the computer's performance further, an "ideal" set of symptoms for each of the diseases was presented to the computer. The ideal symptoms consisted of findings which we felt were typical for the patient with the "classical clinical picture." In every instance, the correct or anticipated diagnosis was given the highest probability of all diagnoses considered. Twenty-seven of the 33 disorders had a probability

figure of 0.90 or greater. Ebstein's deformity of the tricuspid valve and truncus arteriosus, two of the less frequently encountered lesions, were given probability ratings of 0.83, and ruptured sinus of Valsalva's probability figure was 0.71. Two lesions, peripheral pulmonary stenosis and aortic pulmonary window, were given less than 0.50 probability. Yet each was listed as the number 1 diagnosis. Bruce, in evaluating our original matrix, found this approach to be workable. He did note some variation in the probability figures supplied in this matrix compared with what he had encountered in a review of a small series of patients evaluated in his laboratory.[1] Gustafson, working with a modification of our original matrix, found that the computer actually exceeded the performance of six examining physicians, which included two pediatric cardiologists.[4]

Catheterization Diagnosis

The other computer program used for the diagnosis of congenital heart disease in our laboratory employs the processing of catheterization data during the procedure. In this program the outputs from the cuvette oximeter and pressure transducer are transmitted directly to the computer, where they are returned immediately to the catheterization room for on-the-spot evaluation. This is referred to as "on-line" processing because the data are fed directly into the computer without intermediate steps such as punched cards, as used in the clinical diagnosis program.

Fig. 6.4 outlines the mechanics of informational flow in this approach. The physician performs the cardiac catheterization in the usual manner. However, instead of recording the data by conventional recording equipment with the aid of a technician, the physician does the recording by means of a remote control station

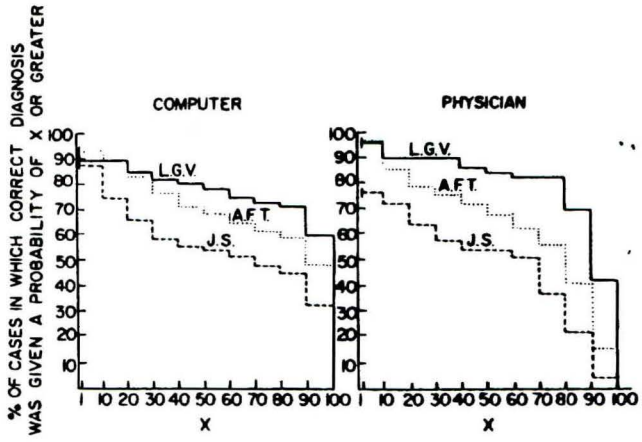

Fig. 6.3. On the abscissa is the probability rating (X) and on the ordinate is the percentage of cases in which the correct diagnosis was assigned a probability of X or greater (From Toronto, A. F., Veasy, L. G., and Warner, H. R. Evaluation of a computer program for diagnosis of congential heart idsease. *Progr. Cardiov. Dis.*, 5: 362, 1963. Reprinted by permission.)

which he runs himself. This control station consists of three basic elements: (1) a memory oscilloscope, (2) a four-digit octal control switch and interrupt button, and (3) a set of amplifiers to transmit the electrical output from the cuvette oximeter, the pressure transducer, and the electrocardiograph into the computer. The control station unit is situated next to the physician so that he can conveniently turn from it to the patient during the catheterization.

The physician communicates with the computer by dialing appropriate numbers on the octal control switch (control panel) which indicate to the computer: (1) the location of sampling site (high atrium, pulmonary artery, femoral artery, etc.), (2) the state of the patient (breathing room air or oxygen, at rest or exercising), and (3) the procedure (oxygen saturation, pressure recording, or indicator dilution curve). The doctor dials these instructions to the computer by means of a specially designed sterile "wand." The computer, in turn, displays to the doctor further coding instructions and/or catheterization data on the memory oscilloscope located in the control station. This information is displayed on the oscilloscope in the form of written messages and numerical values requiring no decoding.

At the beginning of the catheterization procedure the doctor calls the catheterization diagnosis program from the magnetic disc pack into the computer memory unit by dialing the appropriate code number and pressing the interrupt button. When the doctor receives the message on the memory oscilloscope that the program is ready, he dials the code for computer identification of the patient and presses the interrupt button. This procedure then prepares the computer to receive all subsequent data as that belonging solely to the patient being studied. Appropriate calibrations for pressure and oximetry are then entered into the computer and verified by the physician after the calibrations have been completed. The catheterization then proceeds in the usual manner. When an oxygen saturation is desired, the blood sample is withdrawn through the oximeter. By means of the octal control switch, the location of this sample and the state of the patient, along with the oximeter reading, are sent to the computer when the interrupt button is pressed. The computer calculates the percent of oxygen saturation in the sample directly from the electrical outputs from the red and infrared photocells in the cuvette oximeter[16]:

$$\%\ \text{saturation} = \frac{100[HBO_2]}{[HBO_2] + [HB]} = K_1 \frac{\log\left(\frac{''\text{saline}}{''\text{blood}}\frac{-''\text{black}}{-''\text{black}}\right)}{\log\left(\frac{''''\text{saline}}{''''\text{blood}}\frac{-''''\text{black}}{-''''\text{black}}\right)} + K_2 \quad (4)$$

The terms on the left side of this equation are defined as follows: $[HBO_2]$ represents the concentration of oxyhemoglobin and [HB] represents the concentration

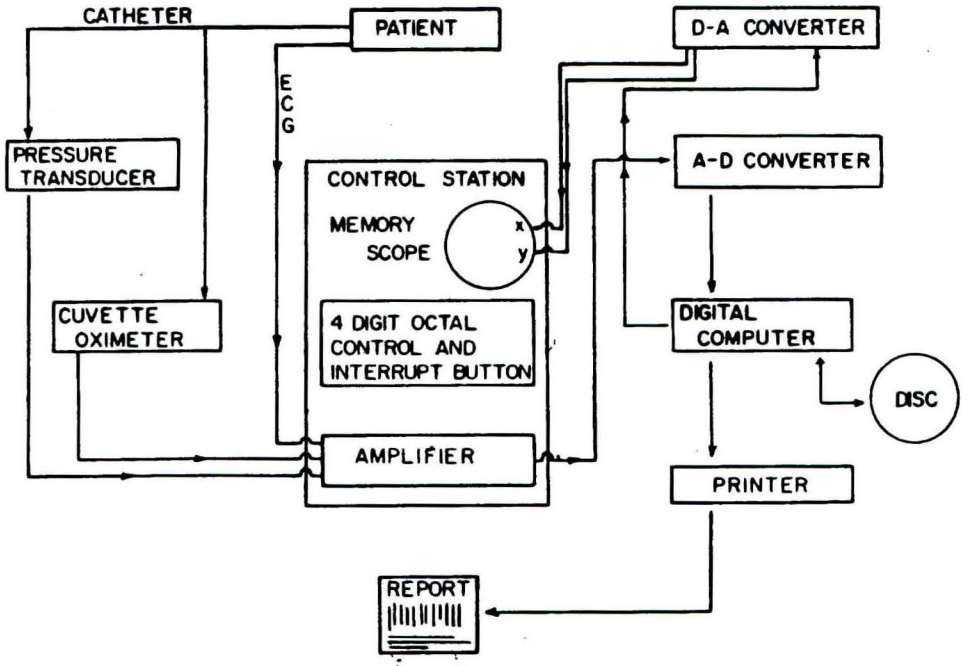

FIG. 6.4. Block diagram outlining the flow of information in the on-line computer processing of cardiac catheterization data.

of reduced hemoglobin. The percent saturation is then defined as the ratio of oxyhemoglobin to total hemoglobin. This ratio can be determined by the electrical outputs from the red and infrared photocells in a cuvette oximeter. Oxyhemoglobin concentration is determined by the amount of light transmitted in the sensitivity range of the red photocell at a wavelength of 640 mμ. At this wavelength the amount of light transmitted by reduced hemoglobin is negligible. Total hemoglobin concentration is determined by the amount of light transmitted in the sensitivity range of the infrared photocell at 800 mμ. At this wavelength, transmission of oxy and reduced hemoglobin is identical.

The terms on the right side of Eq. (4) are defined as follows: R_{saline} is the electrical output from the red photocell in the cuvette oximeter when the photometric chamber is filled with saline; R_{black} is the electrical output from the red photocell with no light transmission (shorted to ground); R_{blood} is the electrical output from the red photocell when blood is in the cuvette oximeter; IR_{saline}, IR_{black}, and IR_{blood} in the denominator are the same terms, representing electrical output from the infrared photocell; and K_1 and K_2 are constants derived for each cuvette oximeter. At the beginning of each procedure the operator causes the computer to read the output of the red cell and infrared cell with saline in the cuvette and again with the output of the photocells shorted to ground. This enters R_{saline}, IR_{saline}, R_{black}, and IR_{black} into the computer for use in Eq. (4) for all subsequent saturation readings. Then with each saturation reading both of these photocells are read by the computer while the blood is flowing through the cuvette and the calculation carried out. The constants K_1 and K_2 are stored on the magnetic disc and need not be introduced separately for each patient. The saturation readings are accurate within 2% from one patient to the next. Any drift in the readings can be detected in a given subject by passing blood which is 100% saturated through the instrument, and corrections can then be introduced into all readings very easily through the final edit routine described below.

Gradients in oxygen saturation caused by left to right shunts are recognized by the computer computation of the following equations for the following sampling sites:

1. Right atrium if only a single caval sample is obtained:

$$5\left(\frac{\text{R.A. sat} - \text{caval sat.}}{100 - \text{caval sat.}}\right) \geq 1$$

2. Right atrium with both caval samples:

$$6\left[\frac{\text{R.A. sat.} - \left[\dfrac{(\text{I.V.C. sat})2 + (\text{S.V.C. sat.})}{3}\right]}{100 - \dfrac{(\text{I.V.C. sat.})2 + (\text{S.V. C. sat.})}{3}}\right] \geq 1$$

3. Right ventricle:

$$8\left(\frac{\text{R.V. sat} - \text{R.A. sat.}}{100 - \text{R.A. sat}}\right) \geq 1$$

4. Pulmonary artery:

$$8\left(\frac{\text{P.A. sat.} - \text{R.V. sat.}}{100 - \text{R.V. sat.}}\right) \geq 1$$

These equations function only for computer recognition of left to right shunts and are not utilized for

quantitation. If samples cannot be obtained from both vena cavae, the first equation is used. If we were to assume that the caval saturation were 70% and the right atrial samples averaged 77% the equation would read:

$$5\left(\frac{77-70}{100-70}\right)=\frac{35}{30}$$

Since this value is equal to or more than 1, the gradient in oxygen saturation would be recognized as a left to right shunt. If the right atrial samples averaged 75%, the equation would read:

$$5\left(\frac{75-70}{100-70}\right)=\frac{25}{30}$$

Since this value is less than 1, the computer would not recognize this gradient as a left to right shunt. When both cavae are sampled the second equation is employed. Because the volume of venous return from the inferior vena cava is usually twice that of the superior vena cava, the inferior vena caval sample is given twice the value of the superior vena caval sample. Similarly, with both samples obtained, a smaller oxygen gradient would more likely indicate a left to right shunt and, accordingly, the constant value was raised from 5 to 6. For the same reason, beyond the tricuspid valve where more complete mixing occurs, the constant value is raised to 8 to allow recognition of smaller oxygen gradients.

The utilization of these equations reduces the error introduced by varying cardiac output. Since such calculations are completed in a fraction of a second, the computation of these equations is preferred over the setting of an arbitrary figure such as 5% or 3% for recognition of oxygen gradients. These equations also aid in recognition of relatively small shunts "downstream" from large left to right shunts. Such shunts might be overlooked if an arbitrary figure of 2 or 3% were to be used as recognition of an additional oxygen gradient.

With a similar coding technique, pressures can be analyzed by the computer, reviewed by the physician, and stored for later print-out. Each pressure is analyzed over a 5-sec interval, and the average waveform is displayed on the oscilloscope along with the actual pressures in mm Hg. The averaging of the pressures eliminates artifact from catheter motion and from patient respiratory movement. At the following sites the following pressure parameters are recorded:

1. Atrium, cava, and pulmonary artery "wedge"—a wave peak, v wave peak, and mean pressures.
2. Ventricle—peak systolic, initial diastolic, and end-diastolic pressures.
3. Artery—systolic, diastolic, and mean pressures.

During catheter withdrawal from chamber to chamber, the averaged waveforms can be stored and another subprogram can be called which compares them to obtain mean gradients across the valves and plots the two waveforms, superimposed, both on the memory scope and on the final printed report.

If indicator dilution curves (indocyanine green) are used in the catheterization study, the computer program analyzes the contours for cardiac outputs or shunts. This analysis is also "on-line," enabling the calculated data and the contour of the curve to be displayed back to the physician. Furthermore, any accumulated patient data in this on-line function can be recalled at any time during the procedure for visualization of the memory oscilloscope. In this way the physician doing the catheterization can evaluate the results obtained at any time during the study. If a sample is stored and later found to be technically unsatisfactory or otherwise incorrect, this can be deleted from the stored data and thus from the final report. At the end of the procedure the physician may call for a print-out of the accumulated data in as many copies as he desires. This print-out lists all the findings and summarizes by listing all abnormal findings. The physician then has at the completion of the catheterization what is essentially a complete report of the study. The advantages of this approach in saving professional time are as obvious as they are welcome.

Similar remote control stations may be used outside the cardiovascular laboratory. In the intensive-care area one is to be utilized for bedside monitoring of postoperative cardiac patients. With either coaxial or telephone line connection to the computer and with in-dwelling arterial and venous catheters in the patient, immediate computation of cardiac output, peripheral vascular resistance, and stroke volume can be calculated from instant to instant. Since this type of program involves time-sharing of the computer, other cardiovascular laboratories within Salt Lake City (University of Utah and Holy Cross Hospital) are employing similar remote control stations with telephone line or coaxial connection to the L. D. S. Hospital computer system. Time-sharing as used here means simultaneous use of the computer by more than one program. Since the computer is involved in the calculations of any one program for only a fraction of a second, other programs are delayed so little that the user, such as the physician doing a 2-hour cardiac catheterization, has no appreciation that he does not always have ready access to the computer.

The remote control station may also be used in the clinical diagnosis program described earlier. In this modified approach, the checkoff list and the punch cards are eliminated. Using this on-line program, appropriate code numbers are dialed so that the symptoms from the checkoff list are displayed on the scope in sequential groups of five to seven at a time. The physician reviews the displayed symptoms and "marks" those in the group he considers to be present by coding in the appropriate symptom number. He then presses the interrupt button, which marks the selected symptom with an asterisk. He can call for the

next group of symptoms by dialing "0000" on the control switch and pressing the interrupt button. The remaining groups of symptoms in sequence are called, marked, and stored until the checkoff list has been completed. At this point the code for the print-out is dialed and the interrupt button is pushed. The symptoms checked and differential diagnoses with their probability figures are printed out, both on the memory scope and on the printed report.

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