MEDICAL GRAND ROUNDS
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STRESS TESTS AND CORONARY DISEASE

THERE MAY BE NO "OBJECTIVE ABNORMALITIES" IN FROM 25 PER CENT (BIÖRCK, 1946) TO 75 PER CENT (FRIEDBERG, 1956) OF PATIENTS WHO HAVE RECENTLY DEVELOPED SIMPLE ANGINA PECTORIS. STRESS TESTS, DESIGNED TO PRODUCE SPECIFIC SYMPTOMS OR CHANGES IN ECG ARE USEFUL, ACCORDING TO FRIEDBERG, "...IN PROBLEMS OF INSURANCE AND MEDICOLEGAL PRACTICE BECAUSE OF THE POSSIBILITY THAT A HISTORY OF ANGINA PECTORIS MAY BE FABRICATED."

THERE IS NO STRESS TEST THAT IS AS USEFUL, OR AS OBJECTIVE, IN THE DIAGNOSIS OF CORONARY DISEASE AS CAREFUL HISTORY COMBINED WITH RESTING ECG (12 LEADS), PHYSICAL EXAM, X-RAYS, AND LABORATORY STUDIES, IN THAT ORDER. PATIENTS ARE, IN FACT, CONDUCTING THEIR OWN STRESS TESTS CONSTANTLY; MEALS, DAY-TO-DAY WORK EXPERIENCE, EMOTIONAL CRISES ARE SELF-ADMINISTERED STRESS TESTS AND USUALLY YIELD DIAGNOSTIC INFORMATION. THEORETICALLY, IT SHOULD BE POSSIBLE TO ADMINISTER AN EXACTLY MEASURED AMOUNT OF STRESS AND READ OFF A VERY PRECISE ANSWER (POSITIVE OR NEGATIVE) IN TERMS OF CHANGE IN ECG, PULSE RATE, BLOOD PRESSURE, OR A CHEMICAL CONSTITUENT OF THE BLOOD. IN PRACTICE, THERE IS NO SUCH STRESS TEST AS YET.

ONE FORM OF STRESS TEST THAT CAN BE MENTIONED AND THEN QUICKL DISCARDED IS THE ANOXEMIA (HYPOXEMIA) TEST, IN WHICH A PATIENT BREATHES A MIXTURE OF 12 PER CENT OXYGEN AND 88 PER CENT NITROGEN FOR 20 MINUTES. THE END-POINT IS AN ELECTROCARDIOGRAPHIC ONE WHICH IS NEITHER VERY SPECIFIC NOR DISCRIMINATIVE (LEVY, ET AL, 1938; BIÖRCK, 1946; EVANS AND BOURNE, 1941; KOUNTZ AND HAMMOUDA, 1932). THE TEST IS NOT WITHOUT SOME DANGER AND HAS NEVER BEEN IN WIDESPREAD USE.

TESTS UTILIZING EXERCISE STRESS ARE IN COMMON USE, THE MASTER TWO-STEP TEST ESPECIALLY. THEY REQUIRE MORE CAREFUL CONSIDERATION. FRIEDBERG'S COMMENT, HOWEVER, IS VERY APPROPRIATE THROUGHOUT ANY SUCH CONSIDERATION: "ONE DIFFICULTY...IS THE TENDENCY OF THE INVESTIGATOR TO USE THE TESTS, WHOSE VALUE IS STILL SUB JUDICE, AS THE FINAL DETERMINANT AS TO WHETHER THE PATIENT DOES OR DOES NOT HAVE CORONARY INSUFFICIENCY." THE TESTS ARE ACCESSORY BUT NOT DECISIVE, ACCORDING TO FRIEDBERG.

THE MASTER TWO-STEP TEST REALLY BEGAN IN 1929 (MASTER AND OPPENHEIMER) WHO DREW ON EARLIER WORK BY RAPPORT (1917) WHO SUPPLIED THE 9 INCH STEP, AND WILSON (1921). THE 1929 PAPER DESCRIB THE TEST IN ITS PRESENT FORM BUT THE END-POINT WAS NOT ELECTROCARDIOGRAPHIC; NORMAL AND ABNORMAL RESPONSES WERE JUDGED BY THE LENGTH OF TIME IT TOOK PULSE AND BLOOD PRESSURE TO RETURN TO NORMAL AFTER THE TEST. THE TEST REQUIRES THE PATIENT TO GO UP AND OVER 2 STEPS (9 IN. + 9 IN., OR TOTAL RISE OF 1 1/2 FEET) A CERTAIN NUMBER OF TIMES IN 1 1/2 MINUTES. THE NUMBER IS ADJUSTED TO THE PATIENT'S AGE, SEX, AND TOTAL BODY WEIGHT. "NORMAL" TOLERANCE, IN NUMBER OF ASCENTS, WAS DETERMINED ON A GROUP OF NORMAL SUBJECTS; THAT LOAD WHICH WAS ASSOCIATED WITH DELAYED RETURN OF PULSE RATE AND BLOOD PRESSURE WAS NOTED AND THE LOAD JUST BELOW IT WAS TAKEN AS NORMAL. PULSE RATE WAS EXPECTED TO BE WITHIN 5 BEATS PER MINUTE OF THE RESTING VALUE AND BLOOD PRESSURE TO WITHIN 5 MM. (SYSTOLIC) OF RESTING, 5 MINUTES AFTER CESSATION OF EXERCISE. THE TEST, THEREFORE, AND THE TABLES BUILT UP FOR DETERMINING THE NUMBER OF ASCENTS ORIGINALLY HAD NOTHING TO DO WITH ELECTROCARDIOGRAPHIC CHANGES. IT WAS APPARENTLY ORIGINALLY CONCEIVED AS A ROUGH, NON-SPECIFIC SCREENING TEST WHICH HAD NO PARTICULAR RELEVANCE TO CORONARY DISEASE. MASTER'S NEXT ACCOUNT (1935) STILL DOES NOT BRING IN THE ECG AND STILL TREATS THE TEST AS A ROUGH SCREENING DEVICE. IT WAS THE PAPER BY MASTER, FRIEDMAN AND DACK (1942) THAT ABRUPTLY SWITCHED FROM PULSE AND BLOOD PRESSURE CHANGE TO ECG CHANGE, WITHOUT ALTERING THE TEST ITSELF IN THE SLIGHTEST. IN THIS PAPER, MASTER ET AL LAID DOWN THE DICTUM THAT "DEPRESSION OF THE RS-T SEGMENT MORE THAN 0.5 MM. BELOW THE P-R SEGMENT OR FLATTENING OR INVERSION OF THE T-WAVE IS ABNORMAL, AND IS INDICATIVE OF CORONARY INSUFFICIENCY." IN SUBSEQUENT PAPERS (1944, 1950, 1953), HE AND HIS COLLEAGUES EXPANDED THIS CRITERION TO INCLUDE 2 MORE: (1) CHANGE OF UPRIGHT T TO FLAT OR INVERTED T IN ANY LEAD; ALSO CHANGE OF FLAT OR INVERTED T TO UPRIGHT T IN ANY LEAD EXCEPT LL III, AND (2) SIGNIFICANT ARRHYTHMIAS, PREMATURE VENTRICULAR BEATS, WIDENING OF QRS, BUNDLE BRANCH BLOCK, LARGE Q WAVES, AV DISSOCIATION OR PROLONGATION OF PR INTERVAL; ALL ARE ABNORMAL. IN 1957, MASTER AND CO-WORKERS STUCK FAST TO THEIR GUNS AND INSISTED THAT THEIR ORIGINAL CRITERIA, ESPECIALLY THE ONE CONCERNING ST SEGMENT LOWERING OF 0.5 MM. OR MORE, WERE CORRECT. THEY COULD "NEITHER EXPLAIN NOR ACCEPT" OPPOSING VIEWS OF WHICH A GREAT MANY WERE BEGINNING TO APPEAR. NOT UNTIL 1959 DID MASTER, WRITING WITH DONOSO, CONCEDE THAT T WAVE CHANGES WERE USUALLY OF LITTLE CONSEQUENCE AND THAT THE CONFIGURATION OF THE DEPRESSED ST SEGMENT WAS IMPORTANT. A SIMPLE JUNCTIONAL DEPRESSION UP TO 1.5 MM. WAS FINALLY ACCEPTED AS BEING OF NO CONSEQUENCE BUT ISCHEMIC DEPRESSIONS OF 0.5 MM. OR MORE WERE REGARDED AS ABNORMAL. BUT HE STILL CLAIMS THAT THE TEST IS POSITIVE IN

97 PER CENT OF PATIENTS WITH CORONARY DISEASE, BY WHICH HE PRESUMABLY MEANS THOSE WHO ARE CLINICALLY DIAGNOSABLE AS SUCH. THIS IS TO BE COMBINED WITH HIS CLAIM THAT THE SINGLE TEST GIVES ABOUT 3 PER CENT "FALSE POSITIVES" AND THE DOUBLE TEST ABOUT 7 PER CENT. THIS, IF TRUE, WOULD MEAN THAT THE TWO-STEP TEST HAS A DIAGNOSTIC ACCURACY FAR EXCEEDING THAT OF MOST OTHER DIAGNOSTIC METHODS. THE CLAIMS WOULD MEAN THAT 9 TIMES OUT OF 10, THE TEST IS CORRECT.

CRITICISM OF THE TEST

THE MOST EXTENSIVE AND AUTHORITATIVE CRITIQUE OF THE TWO-STEP TEST IS BY SIMONSON AND KEYS (1956). SCHERF AND SCHAFFER (1952) ALSO REVIEWED THE WHOLE AREA CRITICALLY AND USEFULLY. YET ANOTHER BASIS FOR SKEPTICISM IS PROVIDED BY SILVER AND LANDOWNE (1953). ALMOST NO ONE SUPPORTS MASTER'S CLAIM IN FULL. HORLICK (1959) RECENTLY DEMANDED MORE RIGID CRITERIA THAN THOSE PROPOSED BY MASTER. OTHER CLINICAL STUDIES ALONG THE SAME LINE ARE DAVIS ET AL (1953), GROSSMAN ET AL (1949), LEEDS AND KROOPF (1953), MASON (1959), MAZER AND REISINGER (1944), THOMAS (1951).

ONE CAN REASONABLY BEGIN A CRITICAL EVALUATION BY QUOTING BIÖRCK'S COMMENT: "THE QUESTION IS, AFTER ALL, NOT TO OBTAIN THE LARGEST POSSIBLE NUMBER OF POSITIVE TESTS BUT TO OBTAIN POSITIVE TESTS WHICH, WITH CERTAINTY, CORRESPOND TO THE PHYSIOPATHOLOGIC CONDITIONS FOR WHICH THE TEST IS INTENDED." IT IS ALSO WORTH NOTING THAT MOST GROUPS OF SUBJECTS STUDIED HAVE BEEN PRESELECTED, EITHER AS NORMAL SUBJECTS OR AS PATIENTS WITH CLINICALLY DISCERNIBLE CORONARY DISEASE. THE QUESTION THEN BECOMES: WHAT, IF ANYTHING, DOES THE TEST ADD OVER AND ABOVE THE INFORMATION GIVEN BY PRIOR METHODS OF SELECTION?

THE STANDARDIZATION OF EXERCISE LOAD, ORIGINALLY DESIGNED ACCORDING TO PULSE RATE AND BLOOD PRESSURE RESPONSE, IS ARBITRARY AND MAY NOT APPLY TO ELECTROCARDIOGRAPHIC TESTS. IT WOULD SEEM THAT THE ORIGINAL DESIGN WAS TO APPLY THE SAME, OR NEARLY THE SAME, WORK LOAD TO EVERYONE (EXPRESSED IN FT.-LBS./MIN.), WITH SOME ALLOWANCE BEING MADE FOR AGE. THE METHOD ASSUMES THAT BODY WEIGHT DUE TO FAT (WHICH IS LARGELY INERT WEIGHT) IS EQUIVALENT TO MUSCLE MASS. THE GRADATION ACCORDING TO ABSOLUTE BODY WEIGHT USED BY MASTER HAS BEEN SHOWN BY SIMONSON AND KEYS TO BE GROUNDLESS. IT SHOULD ALSO BE NOTED THAT THE TEST AS PRESCRIBED BY MASTER MAY EXCEED THE CAPACITY OF SOME PATIENTS AND THUS BE DANGEROUS. FEW DEATHS HAVE ACTUALLY BEEN REPORTED; ROSSIER AND SPÜHLER (1947) REPORTED 3 DEATHS BUT THEIR TEST WAS SEVERE AND POORLY CONTROLLED. MASTER CLAIMS TO HAVE DONE OVER 20,000 TESTS WITHOUT ACCIDENT; IN THE SUMMARY TO THE SAME PAPER, THE NUMBER (WITHOUT ACCIDENT) JUMPS TO 40,000 (1957).

FALSE POSITIVES AND FALSE NEGATIVES. MASTER'S FINDINGS HAVE ALREADY BEEN QUOTED AND ARE DUPLICATED BY NO ONE ELSE. LEPESCHKIN AND SURAWICZ (1958), FOR EXAMPLE, FOUND 26 PER CENT OF 243 PEOPLE, NORMAL TO ALL INTENTS AND PURPOSES, SHOWED POSITIVE DOUBLE MASTER TESTS. IN HORLICK'S STUDY (1959), APPLICATION OF MASTER'S CRITERIA, AND THOSE OF 2 OTHER (MORE CONSERVATIVE) GROUPS TO A MIXED GROUP OF PATIENTS YIELDED THE FOLLOWING:

CRITERIA	POSITIVES
MASTER	37.4 PER CENT
SIMONSON	13.7 PER CENT
KLAKEG	7.6 PER CENT

SOME OF HORLICK'S PATIENTS ACTUALLY HAD CLINICAL CORONARY DISEASE SO THAT THE POSITIVES ARE NOT ALL FALSE. YET THE EFFECT OF THE VARIOUS CRITERIA IS OBVIOUS.

FALSE NEGATIVES ARE ALSO FAR MORE FREQUENT THAN MASTER FINDS FROM A FOURTH TO A HALF OF PATIENTS CLINICALLY DIAGNOSABLE AS HAVING ASHD MAY SHOW NEGATIVE 2 STEP TESTS AND MASTER HIMSELF REPORTS PATIENTS WITH HEALED MYOCARDIAL INFARCTION WHOSE TESTS, ONCE REGARDED AS POSITIVE, LATER TURN NEGATIVE. IT IS VERY DIFFICULT TO DETERMINE WHAT PREDICTIVE VALUE THE TEST ACTUALLY HAS. RESORT MAY BE MADE TO THE EXHIBIT PREPARED BY ROBB AND COLLEAGUES (1958) BUT, IN SO DOING, SERIOUS DIFFICULTIES ARE ENCOUNTERED. THE WALTER REED SERIES QUOTED CONTAINED 836 PATIENTS WHO WERE SUBJECTED TO THE TEST LARGELY BECAUSE OF ANTERIOR CHEST PAIN OR ABNORMALITY OF THE RESTING ECG (83.8 PER CENT IN BOTH CATEGORIES; 15.6 PER CENT WERE DONE BECAUSE OF HYPERTENSION OR NON-SPECIFIC CARDIORESPIRATORY COMPLAINTS; 0.6 PER CENT HAD HEALED MYOCARDIAL INFARCTION). DOUBLE 2-STEP TESTS WERE DONE IN THE PERIOD 1942-1951 AND FOLLOW-UP WAS TO 1952 ANNIVERSARY OF THE TEST. SOME PATIENTS, THEREFORE, WERE FOLLOWED 10 YEARS, SOME ONLY ONE. SOME OF THE RESULTS ARE AS FOLLOWS:

CRITERION	DEATH RATE DUE TO CORONARY DISEAS (PER 1000 PERSON YEARS OF OBSERVATION)	
	NEG. REACTORS	POS. REACTORS
MASTER'S OWN	5.0	27.3
ISCHEMIC SEG.	5.0	49.2
JUNCTION ST	5.0	23.2
T WAVES (MASTER)	5.0	6.6

IT WOULD SEEM, THEREFORE, THAT THE ISCHEMIC SEGMENT CRITERION (MYERS AND TALMERS, 1955; BRODY, 1959) HAS FAIRLY CLEARCUT PREDICTIVE VALUE, USING DEATH RATES AS A REFERENCE POINT. SIMPLE JUNCTIONAL DEPRESSION HAS MUCH LESS AND T WAVE CHANGES NONE AT ALL. IT SHOULD BE REMEMBERED THAT THE ENTIRE WALTER REED GROUP WAS A PRESELECTED ONE AND THAT OTHER CRITERIA, EVEN THE RESTING ECG, MIGHT HAVE SHOWN EVEN MORE IMPRESSIVE PREDICTIVE VALUE. SUCH INFORMATION IS NOT GIVEN BUT, IN AGREEMENT WITH LEEDS AND KROOPF (1953), RESTING ECG'S PLUS ROUTINE HISTORY AND PHYSICAL, MOST PROBABLY DO THE JOB MORE RELIABLY.

RECOMMENDATIONS

1. THE MASTER 2-STEP TEST CAN SAFELY BE CONSIDERED POSITIVE ONLY IF:
   - (A) AN ISCHEMIC SEGMENT DEPRESSION OF 1.5 MM. OR MORE IS SEEN IN ANY LEAD (LL II, V_4, V_5, OR V_6).
   - (B) VENTRICULAR TACHYCARDIA OR PVB'S FROM MULTIPLE FOCI ARE INDUCED BY THE TEST.

2. THE TEST SHOULD NEVER BE USED AS THE DIAGNOSTIC COURT OF LAST RESORT. CANDIDATES FOR LIFE INSURANCE SHOULD EITHER DECLINE THE TEST OR REQUIRE IN ADVANCE THAT CRITERIA OTHER THAN MASTER OWN BE APPLIED. SIMONSON'S, KLAKEG'S OR LEPESCHKIN'S CRITERIA SHOULD SUFFICE TO PROTECT THE CANDIDATE AS WELL AS THE COMPANY.

3. IF THE TEST IS USED, THE FOLLOWING TECHNIQUE IS MANDATORY:
   - (A) PATIENT'S RESTING ECG SHOULD BE NORMAL.
   - (B) THE PATIENT SHOULD BE RESTED, FASTING, AND SHOULD ABSTAIN FROM SMOKING (OR DRUGS OF ANY SORT) FOR AT LEAST AN HOUR BEFORE THE TEST IS DONE.
   - (C) FULL RESTING ECG MUST BE DONE, ALONG WITH PULSE AND BLOOD PRESSURE, JUST BEFORE THE TEST.
   - (D) MASTER'S STAIRCASE, WITH 9-INCH STEPS, MUST BE USED.
   - (E) THE NUMBER OF TRIPS MUST BE READ OFF MASTER'S TABLES, INADEQUATE THOUGH THEY BE.
   - (F) BEGINNING NO MORE THAN 20 SEC. AFTER CESSATION OF EXERCISE, THE FOLLOWING LEADS (2 OR 3 COMPLEXES EACH) SHOULD BE RECORDED IN THIS ORDER: LL II, V_4, V_5, V_6.
   - (G) SECOND AND THIRD RECORDS SHOULD BE TAKEN AT 3 AND 8 MINUTES AFTER CESSATION OF EXERCISE.

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