## JOINT ANNUAL CONGRESS OF S A PHARMACOLOGICAL SOCIETY, PHYSIOLOGICAL SOCIETY OF SOUTHERN AFRICA AND BIO-MEDICAL ENGINEERING SOCIETY OF SOUTH AFRICA: 15 OCTOBER 1980

MNR DIE PRESIDENT

EK BEGROET U, ASOOK AL DIE KONGRES-GANGERS, MET DIE GOEIE NUUS DAT EK BY HIERDIE GELEENTHEID GEEN POGING GAAN AANWEND OM 'N GELEERDE REFERAAT AAN U VOOR TE DRA NIE. IN DIE EERSTE PLEK SOU DIT 'N MISBRUIK VAN VOORREG WEES DEUR EEN WAT NET GEVRA IS OM U KONGRES TE OPEN, EN TEN TWEEDE SOU EK DIT NOULIKS KON WAAG OP 'N GEBIED WAT VIR MY SO ONBEKEND IS SOOS FARMAKOLOGIE.

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AL WAT EK VANDAG WIL DOEN IS OM MET U 'N PAAR GEDAGTES TE WISSEL WAT KOM UIT DIE PERSPEKTIEF VAN 'N BUITESTANDER, MAAR EEN WAT BAIE DEEGLIK BEWUS IS VAN DIE LEWENSBELANGRIKE TAAK WAT VIR DIE MENSDOM VERRIG WORD DEUR DIE FARMAKOLOOG.

Demonstrating, perhaps, the timeless validity of logical thought, I find myself going back through nearly two centuries to quote a few lines from the "Essay on Man" by the poet and moralist, Alexander Pope. The three couplets that I have chosen may appear, at this moment, to have been selected at random and to be unrelated to one another, but I quote them in the sequence of their occurrence in the poem.

THE FIRST: "WHY HAS NOT MAN A MICROSCOPIC EYE?

FOR THIS PLAIN REASON, MAN IS NOT A FLY."

THE SECOND, WHICH FOLLOWS A DISCUSSION OF HUMAN ATTRIBUTES:

"ALL ARE BUT PART OF ONE STUPENDOUS WHOLE,

WHOSE BODY NATURE IS, AND GOD THE SOUL."

AND FINALLY: "KNOW THEN THYSELF, PRESUME NOT GOD TO SCAN,

THE PROPER STUDY OF MANKIND IS MAN."

WHILE POPE, IN WRITING THESE LINES, WAS MORE CONCERNED WITH MORAL VALUES THAN WITH PHYSICAL HEALTH, THE THOUGHTS EMBODIED IN THEM HAVE A CLOSE BEARING ON THE WORK OF THE

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PHARMACOLOGIST AS VIEWED BY THE MAN-IN-THE-STREET. IN HIS EYES, THE PHARMACOLOGIST, WITH HIS INTIMATE UNDERSTANDING OF THE ACTION AND EFFECT OF ANY CHEMICAL SUBSTANCE INTRODUCED INTO ANY PART OF THE HUMAN BODY, IS NOT ONLY THE GUIDE AND ADVISOR TO THE MEDICAL THERAPIST, BUT ALSO THE INDISPENSIBLE PROTECTOR OF THE HUMAN RACE. IN BOTH CAPACITIES, HE HOLDS THE PHARMACOLOGIST RESPONSIBLE FOR ANY SERIOUS MISCARRIAGE OF DRUG THERAPY THAT MAY OCCUR. FOR WHILE THE DOCTOR AND THE PHARMACIST, IN THE PRESCRIPTION AND FORMULATION OF DRUGS, MUST PERFORCE RELY ON THE PRIMA FACIE EVIDENCE PROVIDED BY THE APPEARANCE AND DISAPPEARANCE OF OBSERVABLE SYMPTOMS, THE PHARMACOLOGIST ALONE CAN PROBE MORE DEEPLY TO DETERMINE THE EXACT EFFECT AND ACTION OF A SUBSTANCE ON HUMAN TISSUE AND ORGANS, INCLUDING ANY EFFECT THAT HAD NOT BEEN INTENDED OR ANTICIPATED BY THE PRESCRIBER OR PRODUCER, IN OTHER WORDS, THE POSSIBLE SIDE-EFFECTS OF A DRUG.

THE LAYMAN KNOWS THAT PHARMACOLOGISTS ARE SURE TO TEST ANY NEW DRUG, AND TO STUDY ITS ACTION VERY CAREFULLY. HE ALSO KNOWS THAT, IN ORDER NOT TO RISK HUMAN LIFE AND HEALTH UNNECESSARILY, SUCH TESTS WILL, IN THE FIRST PLACE, BE CARRIED OUT ON TEST-ANIMALS. AND THE LAYMAN SHARES WITH THE PHARMACOLOGIST THE REALIZATION THAT RESULTS OBTAINED IN ANIMAL-EXPERIMENTS ARE OF ONLY PUTATIVE VALIDITY WHEN TRANSLATED TO HUMAN BEINGS. EVEN WHEN DUE ALLOWANCE HAS

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BEEN MADE FOR COMPARATIVE MASS, AND FOR THE LENGTH OF THE HUMAN DIGESTIVE TRACT, NUMEROUS DIFFERENCES STILL REMAIN TO SUPPORT POPE'S DICTUM THAT "MAN IS NOT A FLY". AND THUS, SINCE ALSO IN PHARMACOLOGY "THE PROPER STUDY OF MANKIND IS MAN", THE ANIMAL-TESTS MUST OF NECESSITY BE REPEATED ON HUMAN BEINGS. AND IT IS HERE THAT THE LAYMAN BEGINS TO HAVE MISGIVINGS AS TO WHETHER IT IS EVEN POSSIBLE, LET ALONE USUAL, FOR ADEQUATE TESTS TO BE CARRIED OUT ON HUMAN BEINGS.

ON THE FACE OF IT, HE HAS GOOD REASON TO DOUBT WHETHER HUMAN GUINEA-PIGS COULD EVEN BE AVAILABLE TO THE AVERAGE PHARMACOLOGIST IN THE LARGE NUMBERS THAT WOULD BE

REQUIRED, IN ACCORDANCE WITH STATISTICAL NORMS, TO REDUCE THE PROBABILITY OF ERROR OR CHANCE TO ZERO, OR AS NEAR TO IT AS MAKES NO DIFFERENCE. THE OCCURRENCE OF SERIOUS SIDE EFFECTS IN I% OF ALL PATIENTS USING A DRUG MAY NOT REVEAL ITSELF IN A TEST GROUP OF EVEN 200, SINCE THE LAW OF AVERAGES DOES NOT OPERATE IN NEAT PATTERNS BUT, RATHER, IN HAPHAZARD EXPERIENCE. FURTHERMORE, TO BE TRULY ADEQUATE, HUMAN TESTS WOULD REQUIRE A NUMBER OF SEPARATE TEST GROUPS DRAWN FROM DIFFERENT CLASSES AND 'CONDITIONS' OF MEN. OBVIOUSLY, THE NUMBER OF HUMAN VOLUNTEERS REQUIRED FOR THE ADEQUATE TESTING OF ONLY ONE DRUG REPRESENTS CONSIDERABLE CROWD AND, IN MANY CASES, THIS MEANS A CROWD ALL SUFFERING FROM THE SAME CONDITION.

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A SECOND CAUSE OF MISGIVINGS ON THE PART OF THE LAYMAN IS RELATED TO THE LIFE-SPAN OF MAN AS COMPARED WITH OTHER MEMBERS OF THE ANIMAL KINGDOM THAT ARE COMMONLY USED AS TEST-ANIMALS. IT IS SELF-EVIDENT THAT CERTAIN LONG-TERM EFFECTS OF DRUGS CAN NEVER BECOME PERCEPTIBLE TEST-ANIMALS WITH A SHORT LIFE EXPECTANCY, BUT COULD MANIFEST THEMSELVES MUCH LATER IN THE LONGER LIFE-SPAN OF THE HUMAN BEING. ONCE AGAIN THEREFORE, ALSO IN THIS RESPECT, "THE PROPER STUDY OF MANKIND IS MAN". BUT HOW, ASKS THE LAYMAN, COULD SUCH LONG-TERM EFFECTS BE FULLY INVESTIGATED BY THE PHARMACOLOGIST IN ANY SHORTER TIME THAN THE AVERAGE HUMAN LIFE-SPAN? AND IS ANY WOULD-BE PRODUCER OF A DRUG PREPARED TO LAUNCH SUCH LONG-TERM PHARMACOLOGICAL TESTING OF HIS DRUG SO THAT IT MAY BE MARKETED BY THE NEXT GENERATION? IF NOT, IS THERE EVER COMPLETE CERTAINTY THAT THE BENEFICIAL USE OF A DRUG FOR MANY YEARS MAY NOT BE STEERING TOWARDS A GHASTLY MOMENT OF DISILLUSIONMENT AND DOOM FOR, PERHAPS, MILLIONS OF PEOPLE? UNLESS HE IS USING ONLY DRUGS OF CONSIDERABLE ANTIQUITY, THE LAYMAN MAY WELL HAVE GOOD REASON TO FEEL THAT HE IS ONE OF THE TEST-ANIMALS.

BUT, APART FROM THE NEED TO CONDUCT TESTS ON AN ADEQUATE NUMBER OF PEOPLE AND OVER AN ADEQUATE PERIOD OF TIME, THERE IS ALSO THE NEED FOR TESTING IN AN ADEQUATE VARIETY OF CIRCUMSTANCES. THE FACT THAT "MAN IS NOT A FLY" REFERS

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NOT ONLY TO THE EXISTENCE OF PHYSICAL DIFFERENCES, BUT ALSO TO THE FACT THAT SUCH PHYSICAL DIFFERENCES ARE NECESSARY TO ACCOMMODATE THE DIFFERENT NEEDS, ENVIRONMENTS AND HABITS THAT SET APART THE DIFFERENT SPECIES OF ANIMAL LIFE. IF AN ANIMAL IS ALLOWED FREE ACCESS TO EVERY FORM OF NOURISHMENT AVAILABLE ON EARTH, IT WILL USUALLY CHOOSE A DIET THAT COULD BE RECORDED IN A FEW LINES OF WRITING, BUT MANY CHAPTERS WOULD BE REQUIRED TO LIST THE SUBSTANCES, COMBINATIONS OF SUBSTANCES, AND ALSO THE UNENDING PERMUTATIONS OF COMBINATIONS THAT MAKE UP THE DIET OF MAN. A COMPARISON OF LIQUIDS IMBIBED WOULD BE NO LESS REMARKABLE.

ALL THIS, THE LAYMAN KNOWS, IS COMMON KNOWLEDGE TO THE PHARMACOLOGIST, WHO CAN BE EXPECTED TO TAKE GREAT PAINS TO PREDICT OR IDENTIFY INCOMPATIBILITIES BETWEEN THE VARIETY OF MEDICINAL AND NUTRITIVE SUBSTANCES INGESTED BY MAN. BUT WHAT THE LAYMAN HAS GOOD REASON TO DOUBT IS WHETHER THE SCOPE OF TESTING COULD HAVE EVEN THE REMOTEST HOPE OF CATERING FOR ALL THE COMBINATIONS AND PERMUTATIONS THAT FORM PART OF THE DAILY EXPERIENCE OF MANKIND. ADD TO THIS THE IMPACT ON THE HUMAN BODY OF A WIDE RANGE OF ACTIVITIES AND ARTIFICIAL ENVIRONMENTAL FACTORS THAT ARE UNKNOWN IN THE EXPERIENCE OF LESSER ANIMALS, AND THE IMPROBABILITY OF FOOL-PROOF TESTING IS STRONGLY REINFORCED.

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FINALLY, WE ARE ADVISED BY POPE TO SEE ALL OF THE HUMAN BODY, TOGETHER WITH THE SOUL, AS FORMING "ONE STUPENDOUS WHOLE". AND THE LAYMAN OFTEN WONDERS PHARMACOLOGIST IS ALWAYS CONSCIOUS OF THE FACT THAT EVEN THE LITTLE PATCH OF TISSUE BEING STUDIED BY A MOLECULAR PHARMACOLOGIST MUST BE SEEN AS A SECTION OF THE TOTAL BODY WHICH SHARES IN THE EXPERIENCE OF ANY OF ITS PARTS. AND THE PHYSICAL EXPERIENCE OF MAN IS TRANSLATED INTO A MENTAL AWARENESS AND AN EMOTIVE PSYCHOLOGICAL REACTION. IT TOOK THE MEDICAL PROFESSION A LONG TIME TO REALISE THAT A MAN IRON LUNG, ALTHOUGH RECEIVING AN ADEQUATE OXYGEN INPUT, STILL SUFFERED VERY SEVERE PSYCHOLOGICAL DISTRESS BECAUSE THE ACCUSTOMED MOVEMENT OF THE THORAXIC CAVITY HAD BEEN ARRESTED. SIMILARLY, MANY PATIENTS IN THE PROCESS OF EXCELLENT RECOVERY FROM A CONDITION BEING TREATED BY DRUG THERAPY MAY BE SUFFERING PHYSICALLY AND MENTALLY BECAUSE OF AN OVERALL DEBILITATING EFFECT OF THE MEDICINE OR SOME OTHER UNEXPECTED MANIFESTATION OF ITS ACTION. THIS IS OFTEN, TO THE PATIENT, A TOTALLY UNEXPECTED EXPERIENCE NOT MENTIONED OR WARNED AGAINST IN THE INFORMATION PRINTED ON THE CONTAINER, OR MENTIONED BY EITHER DOCTOR OR PHARMACIST. THE LATTER, IN FACT, MAKES A PRACTICE - FOR SOME OBSCURE REASON, OF REMOVING THE LITERATURE OFTEN PROVIDED BY THE MANUFACTURER. AND BECAUSE NOBODY TOLD HIM TO EXPECT IT, THE UNHAPPY EXPERIENCE OF THE PATIENT SUGGEST TO HIM A SERIOUS FLAW IN THE DRUG OR THE COURSE OF TREATMENT PRESCRIBED.

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THERE ARE TWO WAYS IN WHICH AN AUDIENCE OF PHARMACOLOGISTS COULD REACT TO THE THOUGHTS THAT I HAVE EXPRESSED TODAY. YOU MAY CHOOSE TO AGREE THAT THE TESTING AND SCREENING OF DRUGS BY YOUR PROFESSION CAN AT BEST PROVIDE ONLY A QUALIFIED ASSURANCE TO THE USER, BUT THAT THE RISKS THAT COULD BE PRESENT ARE OUTWEIGHED BY THE BENEFITS THAT SHOULD BE DERIVED BY THE PATIENT. OR YOU COULD SAY THAT THE MISGIVINGS OF THE LAYMAN, AS I HAVE DEPICTED THEM, ARE GROUNDLESS AND BASED ON PURE IGNORANCE.

BUT WHICHEVER ANSWER YOU CHOOSE TO GIVE WILL AUTOMATICALLY SUPPORT A CONTENTION THAT THERE IS A CRYING NEED FOR BETTER COMMUNICATION BETWEEN THE PHARMACOLOGIST AND THE

PUBLIC. INDEED, THE EXISTENCE OF A COMMUNICATION GAP IS ALMOST INEVITABLE, SINCE YOUR WORK IS NOT PERFORMED UNDER THE GAZE OF THE PUBLIC, AND YOUR PUBLICATIONS ARE DIRECTED MAINLY AT A PROFESSIONAL READERSHIP. BUT THE PUBLIC IS ENTITLED TO AN UNDERSTANDING OF PHENOMENA THAT ONLY THE PHARMACOLOGIST CAN HELP THEM TO UNDERSTAND, AND YOUR PROFESSION WOULD RENDER A GREAT SERVICE TO HUMANITY BY FINDING SOME WAY OF ACHIEVING THIS UNDERSTANDING.

I AM HAPPY NOW, WITH MY BEST WISHES FOR ITS FRUITFULNESS,
TO DECLARE YOUR CONFERENCE DULY OPENED.

D S Henderson 15 October 1980