

VOLATILE ANAESTHETICS

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THE BRILLIANT FRENCH MATHEMATICAN AND PHILOSOPHER
DESCARTES WROTE **"IF THERE IS ANY POSSIBLE MEANS OF INCREASING THE
COMMON WISDOM OF MANKIND, IT MUST BE SOUGHT IN MEDICINE."** THIS
IS AN UNUSUAL STATEMENT FOR ITS TIME SINCE PHILOSOPHERS WERE
MUCH MORE CONCERNED WITH THINGS OTHER THAN MEDICINE AND TO THE
DEGREE THAT MEDICINE MATTERED IT WAS, IN THE MAIN, AS
ILLUSTRATIONS OF PHILOSOPHICAL POINTS OR AS PART OF THE BUSINESS
OF ACHIEVING THE GOOD LIFE, WHICH ALSO INVOLVED ACHIEVING AND
MAINTAINING GOOD HEALTH.

ALTHOUGH THERE SEEM TO BE FEW INTERESTS IN A TRUE
PHILOSOPHY OF MEDICINE SINCE GREEK TIMES, THE IMPACT OF MEDICINE
AND THE PREVENTION OF DISEASE, AS WELL AS THE CURE OF DISEASE

HAVE INCREASINGLY BECOME OF SERIOUS INTEREST TO CULTURAL ANALYSTS AND PHILOSOPHICAL MINDS IN OUR SOCIETY TO PROVIDE THOUGHTFUL DIRECTION FOR THE PRESENT AND FOR THE FUTURE. THERE IS CLEARLY A PHILOSOPHY OF SCIENCE, THERE IS A PHILOSOPHY OF LAW, AND TO THE DEGREE IT IMPACTS ON MEDICINE, THERE IS A PHILOSOPHY THAT SEEMS TO BE CONCERNED MOSTLY WITH THE QUESTIONS OF ETHICS, AND IN A RATHER IMPORTANT DEGREE ANESTHESIOLOGY SHARES IN THAT CONCERN.

THE INTERESTS OF OUR GREAT THINKERS IN DEMOCRATIC SOCIETIES ON THE RIGHTS OF MAN AND JUSTICE FOR ALL PEOPLE HAS A DIRECT BEARING UPON WHAT HAPPENS TO US IN THE VARIOUS APPROACHES TO THE CONQUEST OF DISEASE AND TO THE ALLEVIATION OR TO THE CURE OF PAIN. THESE MAJOR ACTIVITIES IN HUMAN WELFARE ARE ALSO PART OF **ANESTHESIOLOGY**.

IT IS ARGUED BY MANY THAT WE HAVE REACHED A POINT OF ANESTHESIA SAFETY WHERE WE SHOULD BE QUITE SATISFIED WITH OUR PROGRESS. THERE ARE THOSE, IN FACT, WHO BELIEVE THAT THE SAFETY ISSUE HAS BEEN SO LARGELY SOLVED AS TO BE TAKEN FOR GRANTED BECAUSE OF THE SUCCESSFUL EDUCATION OF ABLE PEOPLE IN

ANESTHESIOLOGY, AIDED BY EXQUISITELY PRECISE MONITORING SYSTEMS AND BY EFFICIENT ANESTHETIC AGENTS. THIS POINT OF VIEW, BECOMES, IPSO FACTO, A KIND OF CURRENT PHILOSOPHY OF **ANESTHESIOLOGY** - AND IT MAY BE WIDELY ACCEPTED - EVEN BY THIS DISTINGUISHED EUROPEAN ACADEMY OF ANESTHESIOLOGY.

IN DELIVERING THIS LECTURE I CONSIDERED AND REJECTED THE POSSIBILITY OF A HISTORICAL REVIEW OF HOW WE GOT TO THE POINT OF EFFECTIVE ANESTHETIC CARE DUE, IN PART, TO OUR KNOWLEDGE OF **VOLATILE ANESTHETIC AGENTS**. I FELT OUR PURPOSE COULD BEST BE SERVED IN STUDYING THE EVOLUTION OF KNOWLEDGE NOT NECESSARILY OF HISTORICAL FACTS BUT AS A THOUGHT PROCESS ABOUT THE IMPACT AND IMPORTANCE OF THESE AGENTS. I HOPE THAT THIS BRIEF CONSIDERATION WILL BE STIMULATING AND PERHAPS USEFUL TO YOU WHO ARE IN THE FOREFRONT OF THE ACQUISITION OF KNOWLEDGE IN **ANESTHESIOLOGY** AND ITS APPLICATION TO CLINICAL CARE AND ALSO TO THOSE OF YOU MAINLY RESPONSIBLE FOR THE COMPETENT DAILY ANESTHETIC CARE OF SICK PEOPLE.

I SHALL THEREFORE MAKE AN EFFORT TO REVIEW BRIEFLY THE STORY OF **VOLATILE ANESTHETICS** ONLY IN SO FAR AS IT CONCERNS OUR

THINKING ABOUT ANESTHESIOLOGY AS A BROADER SUBJECT.

I SHALL ALSO ATTEMPT SOME CONSIDERATIONS OF THE ROLE OF **INHALATION ANESTHESIA** IN PATIENT CARE AND SPECIFICALLY THE ROLE OF **VOLATILE ANESTHETIC AGENTS** AND POINT OUT SOME OF THE RATIONAL ASPECTS OF THIS APPROACH TO MODERN THERAPEUTICS AS WELL AS A BRIEF DISCUSSION OF THE DEFECTS OF THESE CONCEPTS AND THE **VOLATILE AGENTS**. SINCE NOBODY HAS THE GIFT OF PROPHECY, IT WOULD BE HIGHLY PRESUMPTIOUS OF ME TO ATTEMPT A PREDICTION OF WHAT THE SITUATION WILL BE LIKE EVEN TEN YEARS HENCE, HOWEVER, I WILL TRY TO BE BOLD ENOUGH TO MAKE SOME MODEST EFFORTS AT PREDICTION ABOUT VOLATILE ANESTHETICS AND WHY THEY SHOULD HAVE AN IMPORTANT PLACE IN OUR PRESENT AND FUTURE THERAPEUTIC SYSTEMS IN **ANESTHESIOLOGY**.

MANY OF THE IMPORTANT **INHALATION ANESTHETIC AGENTS** HAVE BEEN **VOLATILE ANESTHETICS** EXCEPT FOR THE WIDELY USED AGENTS **NITROUS OXIDE** AND PREVIOUSLY **CYCLOPROPANE**. THE LATTER IS NOW OBSOLETE BUT WAS VERY USEFUL FOR TWO DECADES ENDING IN THE 1940's. N₂O IS NOW THE SUBJECT OF A NEW CONTROVERSY STIMULATED BY PROFESSOR EGER AND THERE ARE THOSE WHO PREDICT ITS EVENTUAL EVOLUTIONARY DISAPPEARANCE

DESPITE ITS PRESENT COMMON USAGE.

THE DISCOVERY PERIOD OF **ANESTHESIA** IS ASSOCIATED WITH THE USE OF THE ROUTE OF PULMONARY INHALATION, AND LARGELY WITH **VOLATILE ANESTHETICS** EXCEPT FOR NITROUS OXIDE. IT IS NOT RELEVANT TO MY COMMENTS TO BE CONCERNED WITH THE ORIGINAL DISCOVERY OF **ANESTHESIA** FOR OUR PURPOSES TODAY, ALTHOUGH THAT IS OBVIOUSLY AN IMPORTANT CONSIDERATION IN OTHER CONNECTIONS. IT IS OF INTEREST HOWEVER TO ATTEMPT TO SPECULATE SOMEWHAT ON THE CURIOUS HAPPENSTANCE THAT EVEN THOUGH SOME EFFORTS OCCURRED OVER A LONG PERIOD OF TIME, IT WAS REALLY NOT UNTIL THE MIDDLE OF THE 19TH CENTURY - A VERY SHORT TIME AGO AS MODERN HISTORY EXISTS - THAT **VOLATILE ANESTHETICS** WERE INTRODUCED PRODUCING A MAJOR CHANGE IN SO MANY ASPECTS OF HUMAN LIFE, INCLUDING, OF COURSE, OUR OWN FIELD OF **ANESTHESIOLOGY**. THE REASON WHY **VOLATILE ANESTHETICS** WERE USED BY INHALATION WHEN OTHER AVENUES FOR DRUG ADMINISTRATION WERE CLEARLY THE HABIT OF THE TIMES IN MID 19TH CENTURY SOCIETY IS ONE THAT IS SPECULATIVE. HOWEVER, ALL OF THIS OCCURRED DURING THE FERMENT OF THE INDUSTRIAL REVOLUTION IN GREAT BRITAIN, THE SPREAD

OF NATIONALISM THROUGHOUT THE WORLD, BOTH EAST AND WEST, AND AN INTEREST IN THE CHANGING PERCEPTIONS OF THE ROLE OF MAN IN THE UNIVERSE PRECIPITATED BY THE COINCIDENT GREAT SURGE FORWARD IN BIOLOGY WITH THE INTRODUCTION OF THE **THEORY OF EVOLUTION** BY DARWIN. THE DEVELOPMENT OF THE USE OF **VOLATILE ANESTHETIC AGENTS** WAS A PART OF THESE LARGER SOCIETAL FORCES AT APPROXIMATELY THE SAME TIME AND, IN MY VIEW, INTELLECTUALLY RELATED TO THEM. IT IS NO COINCIDENCE THAT THESE DISCOVERIES PROVOKED OPPOSITION AND HOSTILITY IN THE SAME SOCIETAL ESTABLISHMENTS, INCLUDING THE ESTABLISHED CHURCH ESPECIALLY IN BRITAIN, BECAUSE THE INTUITIVE FEELING OF THE POWER STRUCTURE OF THE VICTORIAN WORLD WAS THAT THE WORLD WOULD NEVER BE THE SAME AGAIN AND IT HAS NOT BEEN. THEY WERE CORRECT IN THEIR CONCERNS ABOUT CHANGE.

AFTER THE GREAT INTELLECTUAL FERMENT AT THE BEGINNING CAUSED BY THE DISCOVERY OF **ANESTHESIA**, ESPECIALLY OF **VOLATILE ANESTHETICS**, AND ITS IMMEDIATE PRACTICAL APPLICATION TO THE RELIEF OF HUMAN MISERY AND SUFFERING - ALTHOUGH IT INTRODUCED

SOME UNIQUE SUFFERINGS OF ITS OWN - THERE ENSUED A STRANGELY QUIESCENT PERIOD OF ABSENCE OF DISCOVERY OF NEW AGENTS FOR APPROXIMATELY 80 YEARS. THERE IS NO AGREEMENT ON THE REASON FOR THE TIME GAP IN ATTEMPTS TO DEVELOP NEW **ANESTHETIC AGENTS**. THERE ARE THOSE WHO MAINTAIN THAT THE FIRST **ANESTHETIC AGENTS** WERE OF SUFFICIENTLY GOOD QUALITY TO BE SATISFACTORY FOR MOST SURGICAL PURPOSES, BUT THERE IS ALSO THE POSSIBLE EXPLANATION THAT DESPITE THE WORK OF SUCH PEOPLE AS SNOW AND CLOVER IN BRITAIN AND OTHERS ELSEWHERE THAT **ANAESTHESIA** HAD A LONG WAY TO GO BEFORE IT WOULD BE ACCEPTED AS A PART OF SCIENCE AND EVEN A PART OF RESPECTABLE CLINICAL MEDICINE. I TEND TO SUBSCRIBE TO THE LATTER VIEW MORE THAN TO THE FORMER.

THERE WAS NO GOOD REASON AT THE TIME FOR GOOD MINDS TO GRAPPLE WITH PROBLEMS IN **ANESTHESIA** SINCE THERE WAS NO APPRECIATION OF THE SCIENTIFIC OR CLINICAL IMPORTANCE OF A SPECIALITY THAT WAS TO WAIT FOR ANOTHER APPROPRIATE TIME IN HUMAN AFFAIRS FOR IT TO BE TAKEN SERIOUSLY, DESPITE ITS INITIAL GREAT IMPACT IN THE DISCOVERY PERIOD.

WHATEVER THE EXPLANATION FOR THIS LONG PERIOD OF DELAY, THERE BEGAN IN THE 1930'S TO BE AN ENORMOUS INTEREST IN THE DEVELOPMENT OF **ANESTHESIOLOGY** AND A CONSEQUENT ACTIVITY IN WHICH NEW AND BETTER **ANESTHETIC AGENTS** WERE SOUGHT. TO SOME DEGREE THE DISCOVERY OF THE FIRST IMPORTANT NEW **INHALATION ANESTHETIC AGENTS** AFTER ETHER AND CHLOROFORM NAMELY **ETHYLENE** AND **CYCLOPROPANE**, AROSE FROM THE INTEREST OF THE EARLY **GIANTS IN ANESTHESIOLOGY** IN THE UNITED STATES AND CANADA, AND THEIR ASSOCIATED COLLEAGUES IN PHARMACOLOGY AND SURGERY TO FIND SOMETHING BETTER FOR SURGICAL PATIENTS.

THE DEVELOPMENT OF **CYCLOPROPANE**, A GAS AND NOT A VOLATILE AGENT, IN THE EARLY 1930'S WAS THE FIRST MAJOR ADVANCE IN THIS RESPECT AND IT DID NOT ARISE OUT OF A THEORETICAL AND SCIENTIFIC BASE FOR THE CONSTRUCTION OF A NEW **ANESTHETIC AGENT**, BUT IT DID COME LARGELY AS A RESULT OF EMPIRICAL WORK. THIS NEW **ANESTHETIC AGENT** HAD AN IMPORTANT IMPACT UPON THE STORY OF THE SUBSEQUENT USE OF ALL OF INHALATION ANESTHESIA, ESPECIALLY **VOLATILE ANESTHETIC AGENTS**, EVEN THOUGH IT WAS A GAS, BECAUSE IT HAD A LOW BLOOD SOLUBILITY (A PROPERTY THAT WAS NOT APPRECIATED

UNTIL YEARS LATER), WAS POTENT AND REQUIRED A CLOSED CIRCUIT FOR ITS USE. ITS MINOR EFFECTS UPON THE HEMODYNAMIC ASPECTS OF THE CIRCULATION, DESPITE ITS POTENTIAL FOR ARRHYTHMIA, WERE GREATLY APPRECIATED BY THE CLINICIANS OF THAT TIME.

ONE CAN EVEN ARGUE THAT THE FIRST APPRECIATION OF THE VALUE OF MUSCLE RELAXANTS IN ANESTHESIOLOGY PRESENTED IN THE CLASSIC INTRODUCTORY PAPER OF GRIFFITH AND JOHNSON IN 1942 IN CANADA MIGHT NOT HAVE BEEN SO EASILY ATTAINED UNLESS **CYCLOPROPANE** HAPPENED TO BE THE **ANESTHETIC AGENT** THEY EMPLOYED DURING THE FIRST USE OF MUSCLE RELAXANTS. IN THIS FERMENT OF RENEWED ACTIVITY IN THE SEARCH FOR BETTER **ANESTHETIC AGENTS**, MANY NEW ONES WERE SYNTHESIZED AND PRODUCED, SOME EMPIRICALLY AND OTHERS BY DESIGN. THERE WAS A GENERAL PROBLEM ASSOCIATED WITH ALL OF THEM AND THAT WAS THE FACT THAT THEY WERE EITHER EXPLOSIVE WHEN USED WITH OXYGEN OR THEY HAD TOXIC EFFECTS ON THE LIVER, THE HEART AND THE KIDNEYS CHARACTERISTIC, FOR INSTANCE, OF THE CHLORINATED AGENTS OF THAT PERIOD. IN FACT THE ROUTE OF HALOGENATION IN THE DEVELOPMENT OF NEW **ANESTHETIC AGENTS** WAS BY MANY VIEWED AS IMPROBABLE BECAUSE IT SEEMED AS THOUGH THERE WOULD

BE A BUILT-IN INTOXICATION POTENTIAL WITH ANY HALOGENATED AGENT.

AS OCCASIONALLY HAPPENS IN THE HISTORY OF IMPORTANT HUMAN ENDEAVOR, A TOTALLY SEPARATE ACTIVITY WHICH HAS BEEN UNAPPRECIATED BY MOST OF US UNTIL RECENTLY WHEN DR. BURNELL BROWN DESCRIBED THE WORK OF DR. JOSEPH H. SIMMONS, WHOSE CHEMICAL WORK WAS SO IMPORTANT TO THE DEVELOPMENT OF THE NEXT VERY IMPORTANT CLASS OF **INHALATIONAL VOLATILE ANESTHETIC AGENTS**. THIS MATTER HAD TO DO WITH **FLUORINE** TECHNOLOGY THAT WAS MADE POSSIBLE BY RESEARCH THAT WAS ASSOCIATED WITH THE SEPARATION OF URANIUM ISOTOPES FOR THE DEVELOPMENT OF THE ATOMIC BOMB. GOOD CAN OCCASIONALLY COME FROM EVIL! THE QUENCHING OF FLAMMABILITY WITH THE COMBINATION OF THE USE OF CARBON AND **FLUORINE** WAS THE KEY TO THE DEVELOPMENT OF THE FIRST NEW IMPORTANT NON-INFLAMMABLE POTENT WIDELY USED **VOLATILE ANESTHETIC AGENT** BY RAVENTOS, I.E., **HALOTHANE**. FROM THIS PERIOD IN THE 1950's A VARIETY OF **ANESTHETIC AGENTS** WITH POTENCY AND LACK OF FLAMMABILITY WERE INTRODUCED. THE MOST IMPORTANT OF THESE FOR CLINICAL USAGE WERE **HALOTHANE**, **ENFLURANE** AND MOST READILY **ISOFLUORANE**.

THE DEVELOPMENT OF **HALOTHANE** WAS HAILED BY MOST AS THE ACHIEVEMENT OF THE HIGHEST DEGREE OF SUCCESS IN THAT INHALATION ANESTHESIA NOW BECAME POTENTIALLY NOT ONLY POSSIBLE FOR ALL PATIENTS BUT MUCH SAFER TO ADMINISTER. THE INCREASED EMPHASIS ON INTENSIVE EDUCATION IN THE BASIC SCIENCES RELATED TO **ANESTHESIOLOGY** AND THE APPLICATION OF SCIENCE TO THE CLINICAL SITUATION WAS A CRUCIAL DEVELOPMENT OF THAT TIME AND HELPED MOVE THE USE OF **VOLATILE ANESTHETIC AGENTS** FORWARD IN A REMARKABLY RAPID MANNER.

AS OFTEN HAPPENS WHEN IN THE COURSE OF HUMAN EVENTS ONE THINKS THAT ONE HAS ARRIVED AT A DEFINITIVE GOAL, ESPECIALLY IN MEDICINE, THERE BEGAN TO BE REPORTS OF UNDESIRABLE EFFECTS UPON RESPIRATION AND CIRCULATION WITH HALOTHANE, AND MOST PARTICULARLY BY THE CASE REPORTS OF HEPATIC NECROSIS WHICH RESULTED IN ONE OF THE MOST UNUSUAL MAJOR RETROSPECTIVE STUDIES EVER UNDERTAKEN IN CLINICAL MEDICINE: THE **HALOTHANE** STUDY IN THE UNITED STATES. SIMILAR SMALLER AND, PERHAPS BETTER STUDIES, OCCURRED IN THE UNITED KINGDOM AND OTHER PARTS OF THE WORLD BUT THERE WERE

NAGGING DOUBTS ABOUT **HALOTHANE** AND THE LIVER, ESPECIALLY IN THOSE COUNTRIES WHERE LIABILITY FOR MALPRACTICE OR INJURY TO PATIENTS WAS A MAJOR CONSIDERATION. INTEREST IN SOLVING THIS PROBLEM WITH RESPECT TO THE LIVER INTOXICATION CAUSED BY **HALOTHANE** WAS GREATLY STIMULATED.

THE SEARCH EVENTUALLY LEAD TO THE STUDY OF A SERIES OF HALOGENATED ETHERS. THE TWO MOST IMPORTANT COMPOUNDS, **ENFLURANE** AND **ISOFLURANE** ARE METHYL ETHYL ETHERS AND ARE STEREO/ISOMERS. THEY HAD MOST OF THE HIGHLY DESIRABLE EFFECTS FOR CLINICAL **ANESTHESIA**. AT PRESENT IT IS GENERALLY BELIEVED THAT **ISOFLURANE** APPEARS TO APPROACH THE GOALS THAT ONE LOOKS FOR IN AN IDEAL **VOLATILE ANESTHETIC AGENT**. IT IS NOT EXPLOSIVE NOR FLAMMABLE; IT IS STABLE; IT DOES NOT DEGRADE SIGNIFICANTLY; IT IS NOT BROKEN DOWN BY THE ENVIRONMENTAL INFLUENCES IN ANESTHETIC LOCATIONS AND ITS BLOOD SOLUBILITY IS RELATIVELY LOW. MOST IMPORTANT IS THE FACT THAT THE METABOLISM OF THIS AGENT APPEARS TO BE CONSIDERABLY LOWER THAN THE OTHERS DEVELOPED UP TO THIS POINT AND, IT THEREFORE SUGGESTS A

DIMINISHED POTENTIAL FOR ORGAN INTOXICATION SINCE THE METABOLITES OF **ANESTHETIC AGENTS** ARE OFTEN ASSOCIATED WITH INTOXICATION IN THE MINDS OF MANY OBSERVERS.

LEAVING COSTS AND SIMILAR ECONOMIC FACTORS ASIDE, IT APPEARS AS THOUGH THE MAJOR CRITERIA FOR AN IDEAL **VOLATILE ANESTHETIC AGENT** MAY HAVE BEEN ACHIEVED WITH **ISOFLUORANE** AND THERE ARE MANY WHO BELIEVE THAT THERE IS NO FURTHER PROGRESS POSSIBLE IN THE SEARCH FOR NEW DRUGS OF THIS TYPE.

SINCE THE CONCOMITANT DEVELOPMENT OF EDUCATION IN **ANESTHESIOLOGY** HAS BEEN SO REMARKABLE AND THE QUALITY OF ANESTHESIOLOGISTS SO VASTLY IMPROVED IN RECENT YEARS, IT DOES SEEM AS THOUGH WE HAVE REACHED A PLATEAU OF EXTRAORDINARY KNOWLEDGE, AND AT LEAST TWO ENORMOUSLY EFFECTIVE NEW **VOLATILE ANESTHETICS** EXIST, WHICH APPEAR TO BE SAFER THAN ANY WE HAVE SEEN FROM THE PHARMACOLOGICAL AND TOXICOLOGICAL STANDPOINT.

ONE THEN ARRIVES AT THE QUESTION OF WHETHER ANESTHESIA BY INHALATION OF **VOLATILE** SUBSTANCES IS REALLY THE MOST RATIONAL WAY TO ACHIEVE ANESTHESIA IN THE FUTURE ASSUMING DRUG DEVELOP-

MENT IS NEARLY AS FAR AS IT CAN GO. WITH THE AID OF HIGH TECHNOLOGY AND MONITORING AND THE RELATIVE EASE WITH WHICH PATIENTS' SAFETY CAN BE ACHIEVED, THERE WOULD BE A NORMAL TENDENCY ON THE PART OF MANY TO THINK THAT OUR WORK IS FINISHED AND THAT WE HAVE ONLY TO GO ON TO REFINEMENTS AND WORKING AT THE MARGIN TO IMPROVE COMFORT, EFFICACY AND SAFETY. WORKING AT THE MARGIN IS MUCH LABOR WITH RELATIVELY MODEST RETURN. IT HAS NEVER BEEN AN ATTRACTIVE OCCUPATION FOR CREATIVE MINDS AND IS NOT A TERRIBLY EXCITING ONE FOR PEOPLE OF ABILITY.

WHAT IS NOT YET TOTALLY UNDERSTOOD IS WHAT DIRECTION ONE SHOULD PURSUE TO PROVIDE THE BEST TOTAL ANESTHETIC CARE OF PATIENTS. WHAT IS THE OPTIMUM ANAESTHETIC CARE DURING SURGICAL EXPERIENCES OR SERIOUS ILLNESS, OR PAINFUL CONDITIONS, AND HOW DOES ONE SET ABOUT TO PROVIDE IT?

THERE ARE MANY WHO WOULD BE PERFECTLY CONTENT WITH WHERE WE ARE WITH **VOLATILE ANESTHETIC AGENTS**. HOWEVER, I FEEL THE NEED TO BRING BEFORE THIS DISTINGUISHED AUDIENCE OF THE LEADERS OF EUROPEAN ANAESTHESIOLOGY A FEW QUESTIONS THAT MIGHT

REASONABLY BE ADDRESSED. THEY HAVE TO BE VIEWED OBVIOUSLY AS ONLY SUGGESTIVE AND SPECULATIVE IN NATURE.

SINCE THE BASIC MECHANISM OF ANESTHESIA IS STILL UNKNOWN THERE IS CONSIDERABLE ROOM FOR ATTEMPTING TO MAKE SOME JUDGMENTS ABOUT ASPECTS OF THE ANESTHETIC PROCESS INCLUDING THE ROUTE OF ADMINISTRATION.

ALTHOUGH IT HAS ALWAYS SEEMED SOMEWHAT UNREASONABLE TO ME TO ANESTHETIZE THE BRAIN AND MANY OF THE ORGANS IN ORDER TO OPERATE ON AN UNRELATED ISOLATED PART OF THE BODY, NONETHELESS, THIS IS WHAT WE STILL DO EVERYWHERE. IF WE COULD UNDERSTAND THE MECHANISM OF ACTION OF ANESTHESIA OR AT LEAST THE LOCI IN THE BRAIN WHERE THOSE QUALITIES DESIGNED TO PROVIDE ANALGESIA, SAFETY, COMFORT AND ORGANIC VISCERAL SUPPORT EXIST, WE WOULD NOT BE LEFT WITH THE SAME DEGREE OF EMPIRICISM, AS WE ARE AT THE PRESENT TIME.

WE ARE THEREFORE LEFT NOT ONLY WITH A LARGELY EMPIRICAL SYSTEM WITH PRECISELY DESIGNED ANESTHETIC AGENTS BUT A JUDGMENT AND A DECISION AS TO HOW TO COPE WITH THE CONSEQUENCES OF THAT

EMPIRICISM. THERE ARE TWO INTERESTING CONCEPTUAL ARGUMENTS THAT TAKE PLACE AS TO THE USE OF THE LUNGS AS A PORTAL OF ENTRY FOR ANESTHETIC AGENTS INCLUDING, OF COURSE, THE IMPORTANT VOLATILE ANESTHETIC AGENTS OR THE USE OF SOME OTHER PORTAL OF ENTRY I.E., INTRAVENOUS INJECTION - A SUBJECT UNDER INTENSE SCRUTINY IN MANY LABORATORIES AT PRESENT - DESPITE THE REAL POTENTIAL OF INCREASING ANAPHYLACTOID REACTIONS THEREBY.

INTERESTINGLY ENOUGH, BOTH SYSTEMS ENCOMPASS THE CONCEPT OF A DELAY OF THE DRUG REACHING THE AREA OF ACTION THAT HAPPENS TO BE DIFFERENT FROM EACH OTHER, BUT NONETHELESS IS SIMILAR IN THOUGHT. WITH THE LUNGS THE DELAY REALLY HAS TO DO WITH THE FUNCTIONS OF VENTILATION. THE INHALED AGENTS WILL ULTIMATELY PRODUCE THEIR EFFECTS BY AN INTRAVENOUS ENTRY INTO THE LESSER CIRCULATION, THENCE TO THE HEART AND TO THE BRAIN WHERE PRESUMABLY THESE SUBSTANCES ACT TO PRODUCE THE STATE WE DESIRE.

IF ONE USES THE INTRAVENOUS ROUTE ONE HAS THE DELAY OF GOING THROUGH THE SYSTEMIC VENOUS SYSTEM, THE HEART AND THE

PULMONARY CIRCULATION AND BACK INTO THE SYSTEMIC ARTERIAL CIRCULATION FOR ACTION. THERE IS THEREFORE NOT ONLY A TIME DELAY BUT A POTENTIAL AND ACTUAL INFLUENCE OF THE ANESTHETIC AGENT ON THE ORGANS THAT THE DRUG CONTACTS IN ITS PASSAGE TO THE BRAIN AS THERE IS IN INHALATION ANESTHESIA. IN THE CASE OF INTRAVENOUS INJECTION THERE IS A COMMON PROBLEM WITH THAT OF ANESTHESIA BY INHALATION, AND THAT IS THE FACT THAT REGARDLESS OF THE PORTAL OF ENTRY OF DRUGS, AIRWAY MANAGEMENT AND VENTILATION AND CIRCULATORY SUPPORT ARE ESSENTIAL WITH EITHER SYSTEM.

THE ARGUMENT THEREFORE FOR THE FUTURE OF **VOLATILE ANESTHETIC AGENTS**, UNTIL AND UNLESS SUBSTANTIAL NEW KINDS OF SCIENTIFIC KNOWLEDGE, POSSIBLY FROM MOLECULAR BIOLOGY, ARISE, IS THAT WE SHALL HAVE TO DEAL WITH THE PROBLEMS OF AN AIRWAY, VENTILATION PRESUMABLY PRECISE AND MECHANICAL, AND WE SHALL HAVE TO EDUCATE ALL OF OUR RESIDENTS AND STUDENTS TO UNDERSTAND THE CONSEQUENCES OF THE ANESTHETIC PROCESS AND ITS EFFECT UPON THE VITAL FUNCTIONS OF RESPIRATION AND CIRCULATION.

WERE IF NOT FOR THESE CONSIDERATIONS, A CASE COULD

POSSIBLY BE MADE THAT THE FUTURE COULD LIE IN THE USE OF **NON-VOLATILE** SUBSTANCES AND PERHAPS IT WILL ALTHOUGH I DON'T THINK SO AT THE PRESENT TIME. HOWEVER, AS LONG AS WE HAVE TO DO ALL OF THE THINGS WE MUST DO, WITH THE AIRWAY AND VENTILATION, THERE WILL BE AN IMPORTANT AND PROBABLY CENTRAL PLACE FOR **VOLATILE ANESTHETIC AGENTS** IN CLINICAL ANESTHESIOLOGY. NO SMALL REINFORCING VIEW OF THIS CONCEPT IS THAT IT IS EASIER AND MORE CONVENIENT TO MONITOR ALVEOLAR ANESTHETIC AGENT CONCENTRATIONS THAN CENTRAL VENOUS OR ARTERIAL BLOOD CONCENTRATIONS OF **NON-VOLATILE ANESTHETIC** DRUGS AT PRESENT. THE NET EFFECT IS BETTER CONTROL AND PATIENT SAFETY WITH THE **VOLATILE ANESTHETICS** THAN ANY OTHER CURRENTLY AVAILABLE GENERAL ANESTHETIC METHOD. GIVEN THIS SET OF CIRCUMSTANCES, THE FUTURE OF THE USE OF **VOLATILE ANESTHETIC AGENTS** SEEMS ASSURED FOR SOMETIME TO COME. WE SHOULD, HOWEVER, CONTINUE OUR EXCELLENT EFFORTS TO DEVELOP NON-VOLATILE SYSTEMS TO THE FURTHEST DEGREE POSSIBLE - AS WE AWAIT THE MESSIANIC PERIOD WHEN WE SHALL KNOW HOW ANESTHETIC AGENTS WORK.

SUMMARY

AN ATTEMPT HAS BEEN MADE TO REVIEW FROM HISTORICAL, CULTURAL, AND PHILOSOPHICAL POINTS OF VIEW, THE SCIENTIFIC EDUCATIONAL AND CLINICAL ASPECTS OF THE DEVELOPMENT OF **VOLATILE ANESTHETIC AGENTS** AND THEIR PRESENT ROLE IN THE CARE OF ANESTHETIZED PATIENTS AS WELL AS THEIR POTENTIAL FUTURE USEFULNESS. IT IS SUGGESTED THAT **VOLATILE ANESTHETIC AGENTS** WILL BE EMPLOYED FOR A LONG TIME TO COME. HOWEVER, IT IS ALSO URGED THAT CAREFUL THOUGHT BE APPLIED TO THE RELATIVE ROLES OF **VOLATILE INHALED AGENTS** WITH RESPECT TO **NON-VOLATILE INJECTED ANESTHETICS** IN FUTURE CLINICAL USAGE. FINALLY, IT IS EVIDENT TO THIS OBSERVER THAT PERFECTION HAS NOT BEEN REACHED. WE MUST LOOK, I BELIEVE, TO MOLECULAR BIOLOGY AS A HOPE TO ANSWER THE BASIC QUESTION OF THE MECHANISM OF ANESTHESIA. AT THAT POINT, WE HAVE THE GREAT OPPORTUNITY OF MOVING TOWARD RATIONAL AND PRECISE WAYS TO CARE FOR OUR PATIENTS DURING ANESTHESIA - A MAJOR EVIDENCE OF PROGRESS STILL TO COME.

I TRUST THAT THE BRILLIANT ACHIEVEMENTS OF THE PRESENT
AND THE PAST WILL STIMULATE US TO IMPROVE THE EVENTS OF THE FUTURE
RATHER THAN TO ACCEPT OUR REAL PROGRESS AS FINISHED GOALS.