GULSTONIAN LECTURES

ON THE

PHYSIOLOGICAL ACTIONS AND THERAPEUTICAL
USES OF CONIUM, BELLADONNA, AND
HYOSCYAMUS, ALONE AND IN
COMBINATION WITH OPIUM.*Delivered at the Royal College of Physicians, London.*

By JOHN HARLEY, M.D., F.R.C.P.,

Assistant-Physician to King's College Hospital, etc.

LECTURE III.

*On the Physiological Action and Therapeutical Use of Henbane, alone
and in Combination with Opium; and on the Combined Operation
of Belladonna and Opium.*

HYOSCYAMUS, or its active principle, when given in small doses, and such as are insufficient to produce positive dryness of the mouth, rapidly subdues ordinary excitement of the pulse, and reduces it, within an hour or two, to its slowest rate; that is to say, to that condition in which it may occasionally be found after a long period of complete rest of mind and body. For example, the pulse of a man ordinarily engaged shall be 80. After a small dose of hyoscyamus (one-fortieth of a grain of sulphate of hyoscyamia, or four drachms of tincture of henbane), it will gradually fall to 60 or 50. In another person, whose pulse may be 72, we shall at the end of the same time find it steadily beating about 45. Schroff states that the three-hundred-and-thirty-third of a grain of hyoscyamine reduces the pulse from 79 to 18. In all my experiments with hyoscyamus and its active principle, I have never observed the pulse to fall lower than 42.

After doses (one-sixteenth to one-twelfth of a grain) sufficient to produce complete dryness of the tongue and hard and soft palates, the pulse will generally experience an acceleration of ten or twenty beats, and be increased slightly in force and volume. This change in the pulse will be observed in from ten to twenty minutes after the subcutaneous injection of hyoscyamine; the acceleration does not usually continue for longer than twenty or thirty minutes, and rarely lasts for an hour. Then the pulse slowly declines, and gains a little in force and volume. It usually decreases about five beats for every interval of twenty or thirty minutes, until, at the end of from an hour and a half to two hours, it attains its minimum rate. Apart from these accelerating or depressing effects upon the pulse, the following symptoms will be observed after moderate doses (one-thirtieth to one-twenty-fourth of a grain). In ten to twenty minutes from the time of injection, the tongue more or less completely dry, rough, and brown, the hard and soft palates dry and glazed, excessive giddiness and a weight across the forehead, somnolency, the cheeks occasionally a little flushed, and the membranes of the eye sometimes slightly injected. After continuing for about an hour, these symptoms pass off; and the tongue and hard and soft palates become covered over with a sticky, acid, offensive secretion, agreeing in all respects with that observed after the action of belladonna. The pupils slowly dilate during the latter part of the action of the medicine, and at its close attain their maximum degree of dilatation.

If larger doses than one-twelfth of a grain be given, the above mentioned effects will be increased in degree, and prolonged for two or three hours; and they will be accompanied either by wakeful, quiet, and usually pleasing delirium, with illusions of the sight; or with such excessive somnolency that the patient cannot keep the eyelids raised for a few seconds, but, when aroused, lapses again into a dreamy sleep, broken by occasional mutterings and slight jerking of the limbs. In either case, the power of maintaining the erect posture will be lost, and at best the patient reels like a drunken man.

When taken by the mouth, hyoscyamus, or its active principle, produces exactly the same effects. They are fully developed about an hour after the ingestion of the medicine.

Three ounces of a succus hyoscyami, prepared for me by Mr. Buckle, of 77, Gray's Inn Road, produced effects equal in degree and duration to one-eighth of a grain of the sulphate of hyoscyamia* used subcutaneously. A fluid-ounce of this succus, or of the common tincture, or fifteen

grains of good extract, are about equivalent to the fortieth of a grain of the sulphate introduced by the skin.

Children will usually bear a very large quantity of henbane. I have frequently given a fluid-ounce of the succus, or tincture, to children under 12 years old, with no other effects than an acceleration of the pulse thirty or forty beats, continuing for an hour and then gradually declining; and, towards the end of the action, a moderate dilatation of the pupil. The mouth has remained clean and wet throughout; and there has been no trace of giddiness or sleepiness.

The effect of henbane upon the lower animals is the same as in man. Under the influence of hyoscyamine, the cat becomes dull and lethargic; she walks slowly and clumsily, with the belly near the ground, and loses all spring, and, if placed upon a slight elevation, hesitates so long to jump down, that she eventually slips off the edge and tumbles awkwardly to the ground.

In the dog, precisely the same symptoms are observable; but, in this animal, the medicine appears to have as much influence in accelerating the pulse as atropia itself; and, as far as my experience goes, I should be unable to say whether, in a given case, the animal were under the influence of hyoscyamus or of belladonna. Hyoscyamus does not give so much force to the action of the heart as belladonna does; but this is a difference only to be appreciated by a comparative experiment.

In its action upon the system, hyoscyamus appears to be intermediate between opium and belladonna, possessing as it does, on the one hand, powerful somniferous properties second only to opium itself, and, on the other, an influence upon the sympathetic nervous system, as indicated by the pulse, secondary only when given in larger doses, to that possessed by belladonna itself.

Compared with belladonna, it is distinguished by a preponderance of deliriant or somniferous properties. Compared with opium, it agrees, on the one hand, very closely with that drug in its cerebral effects, provided we take a wide view of the operation of both medicines upon the system; while, on the other, its influence upon the pulse, upon the mucous membrane of the mouth, and upon the pupil, place it in strong contrast with that drug. In addition to its cerebral and sympathetic effects, henbane has a powerful depressant influence upon the motor function, and thus comes into relationship with conium.

I have referred the chief effects of belladonna to its stimulant action upon the sympathetic nervous system; and it cannot be doubted, I think, that the more obvious effects of hyoscyamus arise from the same cause; but the stimulant effect of hyoscyamus is, comparatively speaking, of so short a duration, that this action, as indicated by the condition of the urinary secretion, is not very manifest.

Hyoscyamine, however, like atropia, is eliminated by the kidneys. It may be detected in the urine at any time during the operation of the medicine. I have demonstrated its existence in the urine twenty-two minutes after the injection of one-fifteenth of a grain of hyoscyamine into the skin, and two hours and a half after two ounces of the succus hyoscyami were taken into the stomach. Further, it may readily be isolated from the urine, and identified and distinguished from atropia. The urinary constituents themselves do not appear to undergo any diminution nor increase during the operation of hyoscyamus; this will be apparent by reference to the following analysis.

Fred. C., aged 50, was the subject of neuralgic pain in the neck. I injected one-eighth of a grain of sulphate of hyoscyamine over the spine of the fifth cervical vertebra at 3.48 P.M., three hours and three-quarters after a meal of tea and bread and butter. He urinated last at 2 P.M., two hours after the meal.

Urine passed at the time of injection, two fluid-ounces, specific gravity 1016, strongly acid, pale, remained bright on boiling. 1000 grain measures contained—Chlorine, 4.56 grains; urea, 14.8 grains; phosphates and sulphates, 7.01 grains; uric acid, no excess.

Urine passed three hours and three-quarters after the injection, and at a time when the hyoscyamus symptoms had almost wholly passed off, nine fluid-ounces, specific gravity 1008, and lighter coloured; otherwise agreeing with the previous urine. 1000 grain measures contained—Chlorine, 2.42 grains; urea, 9 grains; sulphates and phosphates, 3.75 grains; uric acid, a mere trace.

The fact of the passage of hyoscyamine and atropia, in an undecomposed state, through the urinary tract in their passage out of the system, leads me to the consideration of the influence of these medicines upon the bladder and kidney itself. At the end of the operation of belladonna or hyoscyamus, many individuals altogether fail to pass a single drop of urine, and this retention is often prolonged for several hours; but never, when the bladder is in a healthy condition, causing any inconvenience. Sometimes, after prolonged efforts, the patient is able to eject a little urine, a few drops at a time. On three occasions, in adult males, I have been obliged to remove the urine, for the purpose of examination, by means of the catheter; in each case, the No. 11 in-

* The sulphate of hyoscyamia used in these investigations was prepared by the lecturer from the seeds of the biennial plant. It was of a light-brown colour, semi-crystalline, and highly deliquescent.

strument passed with the utmost facility, and, on withdrawing the stylet, the urine flowed in a sluggish, powerless stream, and there was little or no indication of any contractile power behind it. It is plain, therefore, that the proper sensibility of the mucous surface of the bladder was blunted by the contact of the atropia or hyoscyamine, and thus the natural stimulus to contraction was removed.

From these facts, we can readily understand the beneficial influence of these medicines upon that irritable condition which keeps the bladder in a constant state of contraction. In all irritable conditions of the kidney, and especially in the oxalic and uric acid diatheses, henbane is invaluable; but I cannot tarry to adduce particular evidence of this statement. Nor will my limited space permit me to say more of the therapeutical use of henbane. I must proceed at once to consider the interesting and important question of the combined action of the two plants—belladonna and hyoscyamus respectively—and opium, within the body.

First, with regard to the *combined operation of belladonna and opium*. There are a number of persons who accept the general statement, deduced from a number of observations the majority of which are very loosely reported, that belladonna is antagonistic to opium, and *vice versa*; and they would not hesitate in a case of poisoning by either of these drugs to give at once an equally poisonous dose of the other as an antidote. I have no time at present to criticise the cases from which such conclusions have been derived; but, feeling that the whole question required most patient and careful examination, I have devoted much time during the past year to its elucidation. My observations have been made upon the horse and dog, and upon man. For an opportunity of investigating the actions of medicine upon the horse, I am greatly indebted to my friends, the Messrs. Mavor of Park Street. With regard to this particular question, Mr. Frederick Mavor and myself made a series of experiments, determining first the separate effects of opium and belladonna, and secondly the combined operation of the same doses.

[The lecturer here described the effects of opium and belladonna, separately and combined, upon the horse, and then proceeded.]

The conclusion to be derived from these experiments is clear, positive, and unmistakable. It is evident, first, that a small dose of morphia, which alone has no appreciable effect upon the horse, will, when combined with a given dose of atropia, not only intensify, but greatly prolong each and all of the effects of the latter medicine; and, secondly, that atropia, on the other hand, greatly prolongs and intensifies the excitement and delirium which are the chief effects of opium upon the horse.

The experiments upon the dog were peculiarly instructive. In the dog, as in man, there are two classes of individuals. In the one class, the hypnotic effects of opium are readily and constantly induced, and, if the dose be sufficient, profound narcotism results. In the other class, it is difficult, and in many cases altogether impossible, to induce sleep or narcotism, by the administration of doses short of those which are required to kill the animal outright. And, in this latter class, opium produces the most distressing symptoms—faintness, prolonged nausea and retching, with intervals of dreamy, delirious somnolency, rarely or never deepening into sleep, which only comes to the exhausted frame after the effects of the drug have passed off.

Two dogs, each representing one of the above described classes, were the subjects of experiment. In one of these, the representative of the former class, the subcutaneous injection of half a grain of acetate of morphia produced, within half an hour, a state of complete narcotism, which continued for three hours and a quarter; after which the animal awoke, and subsequently relapsed into sleep, from which a slight noise would arouse her. In a second experiment, the ninety-sixth of a grain of sulphate of atropia was injected beneath the skin of this same animal, three hours after the previous injection of half a grain of acetate of morphia, and when the narcotic effects were passing off; the pulse 66; respirations 15; pupils contracting to one-seventh and dilating to one-sixth; tongue clean and moist. Eight minutes after the injection of the atropia, the pulse was accelerated 40 beats: in fifteen minutes, 150 beats, and the pupils were dilated to one-fourth, and unaffected by light; respirations unchanged, tongue also unchanged, but soon afterwards the mouth became dry. For three hours after the injection of the atropia, the animal continued in a state of narcotism; and for the next hour this was decidedly deeper than it was previously to the use of the atropia; and, at the end of the three hours, the stimulant effect upon the sympathetic, indicated by acceleration of the pulse and dilatation of the pupil, still continued. In this case, a small dose of atropia deepened the narcotic influence of the opium; while the disproportionately large dose of this latter drug in no way diminished the action of the belladonna.

In another experiment, ten fluid-minims of tincture of opium were injected by two punctures beneath the skin of the same animal. It pro-

duced only a drowsy condition. At the end of two hours, when the drowsiness had so far passed off that the dog would get up and run to the door on the approach of a footstep, and when the pulse was 78, respirations 18, pupils one-sixth, contracting to one-seventh, I injected one-fourth of a grain of sulphate of atropia beneath the skin. Within five minutes, the bitch was in a complete state of narcotism, and continued so, without movement of a limb for the next four hours. Ten minutes after the injection of the atropia, the pulse had gone up to 290 beats, while the respirations had fallen to 16, and the pupils were fully dilated and fixed. An hour after the injection, the nose, tongue, and mouth, were quite dry. I could not arouse her by any noise, or by pushing my finger down to the glottis. Three hours after the injection, the pulse was accelerated 140 beats, respirations 15; she still took no notice when I pinched or pricked her nose or lips, or poked my finger down her throat. She continued sleeping soundly and motionless for three hours more.

Now, in this case, the dose of opium was insufficient of itself to produce narcotism; and it had been previously ascertained that one-fourth of a grain of atropia would not induce a condition at all approaching to it. It is, therefore, conclusive that the atropia increased the narcotic effects of opium; and it is equally clear that the smaller dose of opium altogether failed to depress the atropia action.

In another animal, an excitable Scotch terrier, who may be taken as the representative of the second class, I never succeeded in inducing narcotism by the help of opium alone; and this medicine produced only the most distressing symptoms. Vomiting was the first of these; then followed a restless crying condition, with indications of nausea and headache; constant restlessness, and yet almost an inability to move unless strongly urged to do so; and only short intervals of somnolency constantly interrupted by whining cries. Such was the condition induced by the subcutaneous injection of from half a grain to one grain of acetate of morphia, and it continued for five or nine hours, according to the dose. Now let us consider the *combined operation of morphia and atropia* upon this animal.

I injected one-fourth of a grain of sulphate of atropia beneath the skin, and at the end of one hour and a half the pulse was 200; the pupils were fully dilated, the nose and mouth completely dry; he was quite awake, and alive to all about him, and sitting still; when called, he came up and wagged his tail. At this time, and when he was fully under the influence of the belladonna, I injected beneath the skin two-thirds of a grain of acetate of morphia; he resisted my attempts to do so most vigorously, and made a great noise. No nausea or sickness followed; in three minutes he was completely narcotised and flaccid, and for the next two hours continued in the deepest state of stupor, from which I could not arouse him. At the end of this time he woke up, and, as the atropia symptoms passed off, became very restless and wretched, constantly crying out. After this condition of distress had continued for several hours, I injected the forty-eighth of a grain of atropia, and this was followed by deep sleep, accompanied by the redevelopment of the atropia symptoms, the pulse within twenty minutes being accelerated 125 beats. Here we have a case in which narcotism could only be produced by the combined operation of the two medicines. On one occasion, we see the narcotic effect produced by opium when the system is fully under the influence of atropia; and, at a subsequent stage, we see the same effect produced by atropia at a time when the animal is under the influence of opium alone.

It is quite clear, from these experiments, that in the dog opium and belladonna do but intensify each other's action; and that, while the former has no influence whatever in controlling or altering the action of the latter, atropia actually possesses the power of increasing the hypnotic action of opium. This, it is to be observed, is a conclusion directly the reverse of that accepted by those who believe in an antagonism between opium and belladonna. And it is further to be observed, that this supposed antagonism of belladonna to the hypnotic effect of opium constituted the essence of this belief.

In turning now to the consideration of the combined operation of opium and belladonna in man, I must first concede that belladonna possesses an antagonistic influence to some of the earlier effects of the operation of opium. The first effect of opium, in many animals as well in many of human kind, is a derangement of the vagus nerve, resulting in nausea and retching, faintness, and depression of the heart's action. The dog invariably vomits within five minutes of the subcutaneous use of morphia; and, in my own practice, I have had four or five patients in whom the subcutaneous use of seven drops of laudanum, or of one-twelfth of a grain of acetate of morphia, has produced faintness, nausea, ending in vomiting and retching, with intervals of delirious somnolency for eight or nine hours. By repeated experiments upon these individuals, I have found that the previous or simultaneous use of a small dose (one-ninety-sixth of a grain) of sulphate of atropia

entirely prevents these distressing and often alarming symptoms; and I have even arrested them after they have been fully developed by the subsequent use of the atropia. It is by virtue of its powerful stimulant effect upon the sympathetic nervous system, that the derangement of the vagus nerve, causing the above mentioned symptoms, is overpowered. This is a most important fact; for, by the help of atropia, we may, I believe, bring *all* individuals alike under the beneficial influence of opium. The only question of antagonism that now remains, is that which might be supposed to result from this same stimulant effect of belladonna upon the heart; and it may be asked, "Would not this action alone be sufficient to arouse a patient in whom the pulse and respiration were well nigh obliterated by the effect of opium?"

I answer, inasmuch as belladonna has no stimulant action upon the vagus nerve, and therefore no influence upon respiration, no other result can be expected from the operation of belladonna, in a case of poisoning by opium, than that which would follow its administration in any other similar case of depression of the cardiac and respiratory functions. It will doubtless arouse the heart, but there is little hope of increasing the breathing; while, on the other hand, the atropia, if given in a large dose, will only deepen the stupor. As a cardiac stimulant, the dose should never exceed the ninety-sixth of a grain, repeated at an interval of an hour and a-half or two hours.

With these preliminary remarks I come now to consider the combined operation of opium and belladonna upon man; and I may say, generally, that it is precisely such as I have already described as occurring in the dog. The following experiments, which are in strict accordance with a great number of similar ones made upon almost every variety of constitution, will, I think, when taken with the foregoing experiments upon the horse and dog, conclusively prove that in man also opium and belladonna have not the antagonistic action which has been attributed to them.

1. Samuel M., aged 49, pulse 75, pupils one-ninth, tongue moist. I injected one-quarter of a grain of acetate of morphia into the arm. In one hour, the pulse was accelerated 2 beats, its volume and power unchanged; pupils one-tenth. In two hours, pulse was decreased 9 beats, slightly diminished in volume; pupils one-twelfth. The dose produced a sleepy, tranquilising effect, but he did not sleep nor require to make any effort to keep himself awake, the mouth remained moist throughout.

2. Some days afterwards, I injected the one-forty-eighth of a grain of atropia. In 10 minutes, the pulse was accelerated 45 beats, the pupils slightly dilated, the tongue dry at the tip. In 30 minutes, pulse as last mentioned, pupils one-fourth, tongue dry and brown, hard and soft palates dry and glazed. In one hour, the pulse was accelerated 32 beats; he felt a little dozy; the mouth and pupils were as at 30 minutes. In an hour and 40 minutes, the pulse was accelerated 17 beats; the dryness of the tongue was reduced to a narrow streak; pupils as before.

3. On a third occasion, I injected one-fourth of a grain of acetate of morphia one hour after the injection of the forty-eighth of a grain of sulphate of atropia; when the pulse was accelerated 25 beats, and the pupils dilated to one-sixth; the tongue and palate completely dry. Fifteen minutes after the injection of the morphia, the pulse was accelerated 35 beats; mouth and pupils unchanged; he felt very sleepy. An hour afterwards, the acceleration of the pulse was still 35 beats; pupils one-sixth; the mouth, which had continued parched up to the present time, was moistening; but the back of the tongue and throat were dry and parched. He continued sleeping. In an hour and three-quarters after the injection of the morphia, the pulse was accelerated thirty beats; pupils rather more than one-sixth; mouth moist. He continued sleeping. The effect was charming. He fell off to sleep fifteen minutes after the morphia, and continued to sleep soundly and continuously, breathing 16 tranquilly, by my side, and opposite a bright gas-lamp, for two hours, when I completely aroused him. It is to be observed, on the one hand, that the opium prolonged the belladonna-effects very considerably, while it failed to prevent dilatation of the pupil; and, on the other hand, that the atropia greatly increased the narcotic effects of the opium.

4. On another occasion, I reversed the former experiment on the same individual; and, an hour after the operation of the fourth of a grain of acetate of morphia, when the pulse was accelerated 5 beats; the pupils one-twelfth; respirations 15; the tongue moist and clean; and he was feeling sleepy, but not so much so as to sleep, I injected the forty-eighth of a grain of sulphate of atropia. In twelve minutes, the pulse was accelerated 42 beats, and increased in power; pupils dilated to one-tenth; respirations 14. "He felt heavier for sleep." In thirty minutes, the pulse was accelerated 50 beats; pupils nearly one-seventh; the anterior half of the tongue and the whole of the hard and soft palates were completely dry; the latter glazed. He was sleeping. In one hour, the pulse was accelerated 40 beats; pupils one-seventh; tongue dry and

brown; respirations 12, regular; cheeks and forehead slightly suffused, and warmer; sclerotic a little injected. He was sleeping. In an hour and a half, no change in pulse or mouth; pupils a little larger; respirations 14. He was very sleepy and giddy still, and walked very cautiously. The drowsy feeling, which existed before the injection of the atropia, increased fifteen minutes after the injection of the latter to an inability to keep awake; and he continued to sleep soundly by my side, in front of a bright gas-lamp, for more than an hour, when I was obliged to leave him. He reported that, compared with former injections, he slept unusually soundly the night following this injection; and he voluntarily remarked, that the combined doses had a much more powerful hypnotic effect than the morphia alone. It will further be observed, that the previous operation of the morphia predisposed the system to the influence of atropia, since the effects of this latter were also in this case intensified and prolonged, as will be seen on reverting to Experiment 11.

Opium does not prevent nor retard, so far as I have been able to determine, the elimination of atropia from the system. The following analyses of the urine during the operation of morphia and atropia, successively administered, well illustrates the different actions of these medicines upon the kidney.

Charles V., aged 26, suffering from sciatica. I injected one-fourth of a grain of acetate of morphia at 11.20 A.M., three hours after breakfast. He urinated last directly after breakfast. Fifty-five minutes after the injection of the morphia, one-forty-eighth of a grain of sulphate of atropia was injected.

Urine passed at the time of the morphia-injection, eighteen ounces, specific gravity 1008.0, freely acid. 1000 grain measures contained—chlorine, 2.42 grs.; urea, 6.66 grs.; phosphates and sulphates, 2.33 grs.

Urine fifty-five minutes after the morphia-injection, seven ounces, specific gravity 1007.2, faintly acid. 1000 grains contained—chlorine, 1.82 gr.; urea, 5.66 grs.; sulphates and phosphates, 1.33 gr.

Urine two hours and a quarter after atropia, seventeen ounces and a half, specific gravity 1011.2, moderately acid. 1000 grain measures contained—chlorine, 3.64 grs.; urea, 7.66 grs.; phosphates and sulphates, 2.38 grs.

He could not pass a drop of the atropia-urine. I drew it off with No. 11 catheter. Twelve drops of it, placed at intervals in the eye, caused dilatation of the pupil from one-eighth to one-sixth of an inch for at least four hours.

The combined operation of hyoscyamus and opium presents some interesting features. Briefly, they are as follows. 1. Opium prolongs and intensifies the effects of hyoscyamus, even to producing an acceleration of the pulse some 15 or 20 beats for an hour or more. 2. Hyoscyamus increases the hypnotic action of opium, and to a certain extent is able to prevent the derangement of the vagus nerve, which is frequently the first effect of opium. 3. Opium, given in combination with hyoscyamus, does not prevent the elimination of hyoscyamia by the kidneys.

One word, Mr. President and gentlemen, in conclusion. The study of therapeutics in this country is in a deplorable condition. Expectancy and homœopathy, the twin progeny of ignorance and deception, have grown from a comparatively innocent childhood to most mischievous proportions. But few of us believe in the beneficial action of medicine. Many treat the subject with contempt. Some of our grey-headed practitioners mislead us. We constantly hear them saying, "The longer I have worked and the larger my experience, the less do I rely upon drugs; and I find that I am losing confidence year by year in the action of medicines." What wonder? The same men will tell us that they have never taken particular trouble to ascertain the actions of the medicines they have so long prescribed; and, journeying as they do along a doubtful path, it is indeed no wonder that they should continue to lose confidence, and, in the end, find themselves very far away from the wished for resting-place, to which their tedious and difficult journey ought, with a more careful attention to the landmarks, certainly to have conducted them.

Our working men resort to the microscope; and, deeply engaged in the minutiae there displayed, neglect the better part of their calling, and fall into that *laissez faire* practice which is systematically adopted by some. The dignity of the medical profession is proportionately debased, as it ever must be if we neglect the attentive consideration of those varied and bountiful gifts which Nature has provided to our hands, and adapted, I doubt not, to the necessities of every morbid condition to which the body is liable.

Our medical literature takes so little notice of therapeutical inquiry, that it seems to me essential that something should be done to secure a more general recognition of the importance of this branch of study. The time to cast off our apathy is indeed fully come; and, if we would restore medicine to its true and natural dignity, we must set ourselves earnestly to the work, and labour patiently and perseveringly in that field where I have just now roughly and unskilfully turned over a few clods.