It is, for instance, by no means always easy to distinguish between supra- and infra-phrenic effusions, and, on the right side, abscess between the liver and diaphragm has frequently been mistaken for hepatic abscess—similarly with perinephric abscess. (Cf. an interesting paper by Dr. Hilton Fagge, Guy's Hospital Reports, 1874).

Another point deserving of notice is the remarkable resistance which the two great serous membranes, the pleura and the peritoneum, oppose to the invasion of suppuration from without. Notwithstanding their proximity to a collection of foetid and gangrenous material, and this for a long time, neither membrane was affected to any extent with recent inflammation, and neither serous sac contained fluid.

That extra-pleural abscess may penetrate the pleura appears from an instructive case recorded by Dr. Halley in the "Transactions of the Pathological Society of London, 1855."

ART. VI.—*Chloralamide as a Hypnotic for the Insane.* By GEORGE P. COPE, L.K.Q.C.P., L.R.C.S.I.; Senior Assistant Resident Medical Superintendent, Richmond District Asylum, Dublin.

I OWE my first acquaintance with chloralamide to the good nature of Sir John Banks, K.C.B., who, knowing the interest which we take in the Richmond Asylum in new drugs of the hypnotic class, drew my attention, with his usual kindness, to Drs. Hagen and Hüfler's observations in the *Munchener medicinische Wochenschrift*, No. 30, 1889. My chief was so good as to allow me to apply this drug in any case which I thought suitable. The results have seemed so satisfactory that I am disposed to think it is a valuable addition to our list of soporifics.

Chloralamide is a product of the direct combination of chloral anhydride and formamide in molecular quantities, represented by the formula $\text{CCl}_3\text{H} \begin{smallmatrix} \text{OH} \\ \diagup \\ \text{N} \end{smallmatrix} \text{HCHO}$. In substance it has the appearance of colourless crystals, and is stated to be soluble in nine parts of water. Dr. Casswell Harrison (*The Pharmaceutical Journal*, September 7th, 1889) states:—"I have failed to dissolve 20 grains in 240 fluid grains of water, the actual solubility being about 1 in 14." It is not unpleasant to the taste, although slightly bitter, nor is it astringent. In some instances 25 to 30 grains produced sound and apparently refreshing sleep, but with the majority of the cases which I noted I found that 35 to 45 grains were necessary.

I am not aware of the general use of this medicine in Ireland, but Dr. Paterson, of Cardiff (*The Lancet*, October 26th, 1889), has given an account of the result of its trial in fourteen cases of insomnia, embracing patients suffering from phthisis and heart disease, with very encouraging results. It is important to note that Dr. Patterson observed that chloralamide checked the night sweating of phthisis, and in proof that chloralamide may be safely administered to persons suffering from cardiac disease, phthisis, and pneumonia, I have selected for notice some cases (Nos. 4, 6, 7, 10, 11, 12) in which one of these ailments existed. I have also closely observed the effect of chloralamide as a sleep-producing agent on twenty-five patients suffering from insanity under my immediate care, and the following are brief notes taken by me of the cases which I deemed the most interesting:—

CASE I.—E. H., female, aged twenty-eight, admitted March 5th, 1887. A case of recurrent melancholia. The attacks are characterised by complete absence of sleep, great anxiety, and general restlessness, with suicidal tendencies. Towards the latter end of November, while the patient was suffering from one of these outbursts, I administered 30 grains of chloralamide at 9 o'clock; fell asleep 45 minutes after the draught, and slept six hours. The following night at 8 30 she received the medicine; was asleep at 9 o'clock p.m.; at 2 a.m. she got out of bed. Night nurse reported that patient staggered as if under the influence of drink;^a remained quiet, but did not sleep for the rest of the night. Patient continued receiving this medicine for eight nights consecutively with no bad results. Average time slept, six hours.

CASE II.—M'C., female, aged forty-five, admitted October 25th, 1889. A case of melancholia, with suicidal tendencies. Delusions that she has committed an unpardonable crime; that she is going to be killed; says, "I would prefer to die by my own hands;" has made several attempts to do so; extremely restless, excitable, and devoid of sleep; cannot be kept in bed at night. November 2nd, at 8 30 p.m., she received 3ii. of elixir of chloralamide (30 grains). The draught had the desired effect; the sleep produced was unbroken and natural. Chloralamide was continued for four nights; discontinued two; resumed for eight nights consecutively. Average sleep, eight hours, with no bad symptoms. Patient now sleeps the greater part of the night.

CASE III.—B. H., female, aged thirty-two, admitted October 13th, 1888. A case of melancholia agitata. For some time previous to

^a Dr. Patterson, Cardiff, also noted a similar effect with chloralamide.

admission insane. Hereditary history (mother and sister)—Delusions that she has some dreadful disease; that her body is falling into pieces; continually rushing to and fro, and clinging to the nurses. At night extremely restless and noisy; cannot be kept in bed. Administered 35 grains of chloralamide on November 2nd at 8 30; slept from 9 p.m. until 6 a.m. Continued the chloralamide until November 7th, then discontinued for four nights (sleeping about three hours, afterwards very noisy). Resumed this medicine until the 25th, with an interval of three nights—17th, 18th, and 19th; produced on an average seven hours' quiet sleep, with no bad result.

CASE IV.—M. H., female, aged forty, admitted March 14th, 1889. A case of melancholia with extreme depression and suicidal tendencies. Delusions that her relatives and friends have been killed. About a fortnight after her admission improved considerably, worked in the division, and appeared more cheerful.

November, 1889.—When she was out along with some other female patients, who had the privilege of country walks, she escaped from the attendants and jumped into a pond. The weather being very cold, this escapade was followed by an acute attack of pneumonia. Became extremely restless and sleepless at night. Received 30 grains of chloralamide for five consecutive nights; average result, six hours' sleep. Patient is again mentally progressing towards convalescence.

Sphygmographic tracings, taken before and after chloralamide was received, showed no apparent change in rhythm, or pressure of pulse.

CASE V.—A. H., aged sixty-seven, admitted May 22nd, 1888. An old case of chronic melancholia. Delusions that she has some infectious disease, and that the rest of the patients have contracted the illness. Occasional outbursts occur, characterised by intense restlessness, hand-wringing, and great anxiety, with complete absence of sleep. During one of these exacerbations, 30 grains of chloralamide were given for six nights consecutively, producing about six hours' sleep on an average. Patient suffers from weak action of heart.

Sphygmographic tracings, taken before and after administration of the drug, showed no change.

CASE VI.—A., female, aged thirty-eight, admitted October, 1889. Phthisical, with very feeble circulation; suffers from melancholia; very seldom speaks; would not take food, so that artificial feeding had to be resorted to. At night absolutely sleepless and extremely restless. On November 22nd, at 8 30 p.m., she received 30 grains of chloralamide; slept from 9 15 p.m. until 6 a.m. The medicine was continued for nine nights consecutively, with marked improvement in patient's general condition; average sleep noted is eight hours. Patient continues to sleep without the drug, and sleeps about five hours..

Sphygmographic tracings, taken before and after the drug was received, showed no change. Respiration and temperature the same.

CASE VII.—M. B., female, aged forty-one, has mitral stenosis. A case of chronic mania. Has a very excitable and uncontrollable temper. Occasionally has attacks of maniacal excitement; intensely restless and violent; noisy and sleepless at night. January 4th, 1890, had one of these outbursts. On the 5th and 6th was treated with 30 grains of chloralamide each night; slept seven, and six and a half hours. Since then no return of maniacal fury.

Sphygmographic tracings, taken on the evening of January the 5th, before the drug was administered, and again on the night of the 6th after the draught, showed no apparent change.

CASE VIII.—S. B., female, aged twenty-three, admitted Nov. 2nd, 1889, suffering from acute mania, with intense restlessness; noisy, mischievous, and untidy; unable to work or fix the attention; very garrulous and incoherent; slept badly, and noisy nearly all night. Chloralamide, 35 grains were given on November 4th at 8 40 p.m. Slept from 9 30 p.m. until 12 30 p.m. The following night did not sleep. On the 7th, 48 grains administered. Slept from 11 p.m. to 4 a.m. Drug was continued till the 12th, with no bad result. Nearly six hours' sleep nightly was produced. Since the medicine has been discontinued patient has continued to sleep well, and has rapidly improved. Now convalescent. Sphygmographic tracings taken showed no apparent change.

CASE IX.—C. E., female, aged forty-six, admitted September 7th, 1889, about eight months after childbed. Was nursing her infant up to day of admission. In fair physical health; mentally very depressed and silent. Remained in this condition for over a week, then followed occasional outbreaks of maniacal excitement, violent and destructive, with alternate attacks of depression. At night slept very badly. Chloralamide was administered in 35 grain doses, and continued for five nights with no bad results, patient sleeping on the whole about eight hours nightly.

CASE X.—B. L., female, aged thirty-eight, admitted August 14th, 1888; from childhood suffered from epilepsy; within the last six years, immediately after a fit (which occurs monthly) maniacal outbursts follow, lasting about a week. These attacks are characterised by uncontrollable fury of a homicidal nature, intense restlessness, and want of sleep at night. During one of these outbreaks, occurring in December, 1889, I administered for two nights 35 grains of chloralamide. First night, slept five and a half hours; second, six hours. After this she continued to sleep well, was less refractory, and the attack was of shorter duration. Patient has mitral valve disease.

CASE XI.—M. E. L., female, aged thirty-four, admitted October 26th, 1889. Wretched physical condition; emaciated and anæmic; marked symptoms of phthisis; very maniacal; noisy, destructive, and violent. At night intensely restless and sleepless; cannot be kept in bed. Administered 30 grains of chloralamide at 9 30 p.m. on November 2nd; patient did not sleep. Next night increased the dose by 5 grains; no sleep followed; 48 grains were next given at 9 o'clock p.m. She slept from 9 45 p.m. till 4 a.m. Chloralamide was continued in same dose for four nights, and then discontinued. She has become quiet, and sleeps the greater part of the night.

CASE XII.—A. J., female, aged thirty, some years in the asylum; very weak-minded; sits unoccupied all the day about the wards, taking no interest in her surroundings. Early in January she suffered from an attack of inflammation of the right lung. At night was extremely restless, sleepless, and could not be kept in bed. For two consecutive nights I gave her 30 grains of chloralamide, which produced sleep for about seven hours. Since then the patient continues to sleep the greater part of the night.

CASE XIII.—M. O'N., female, aged thirty, admitted June 22nd, 1889. A case of recurrent mania. During the outbreaks of maniacal excitement, it is with great difficulty she can be controlled. The attacks are characterised by acts of extreme violence; noisy, untidy, and very dirty, with complete absence of sleep. On November 7th she received 45 grains of chloralamide at 8 30 p.m.: was asleep at 9 p.m.; slept until 5 a.m. For five consecutive nights she received 45 grains of chloralamide, producing sleep on an average seven hours, with very good results, cutting short the attack.

CASE XIV.—M. K., female, aged forty-five, admitted November, 1889. A case of acute mania; strong physical condition; extremely violent, noisy, incoherent, and very destructive; complete absence of sleep at night. Was so violent the first two nights she had to be placed in a single room. On the third night of admission was ordered 30 grains of chloralamide, which had no effect. The following night received 45 grains at 8 40 p.m.; slept from 9 30 p.m. until 1 30 a.m.; and, again, from 1 30 a.m. to 3 30 a.m.; noisy afterwards. This dose was continued for six nights, patient sleeping on an average six-hours. Since drug has been discontinued she sleeps the greater part of the night.

CASE XV.—A. B., female, aged forty-two, admitted August 5th, 1887. A case of chronic mania; delusions of persecution, &c.; very irritable and sulky temper; otherwise has her ordinary mental capacity. Lately she has been suffering from hepatic colic, due to the passing of gall stones. To relieve the pain, I treated her with 15 to 20 grain doses of chloralamide

or three days. No relief followed, or sleep supervened. 45 grains of the drug were then given at night. Patient slept five and a half hours.

CASE XVI.—A. K., female, aged fifty, admitted January 7th, 1884. A case of chronic mania; harmless and useful patient; entertained delusions of a religious nature; suffered from cancer of the liver. Some weeks before death complained of acute pain, and was unable to sleep at night. Chloralamide was administered in 15 grain doses three times a day, which did not relieve her sufferings, or produce sleep; 35 grains of chloralamide were then given at night. Patient slept three hours. No ill results followed, but this drug appearing inoperative was not repeated.

CASE XVII.—M'K., female, aged thirty-six, admitted November 10th, 1889, with symptoms of acute mania; noisy, untidy, and very restless; very garrulous and incoherent, mistaking everyone she came in contact with; at night absolutely sleepless, very noisy and restless. On November 13th she received 30 grains of chloralamide at 9 p.m., but no sleep followed; increased the dose to 40 grains the following night. At 9 30 p.m. she got the draught; at 10 30 p.m. was asleep, and continued so until 3 30 a.m. Noisy and restless afterwards. Chloralamide was further increased by 5 grains, and continued three consecutive nights. Sound sleep always followed, lasting about six hours. It was unnecessary to further continue this drug, as she improved rapidly. Left the asylum December 20th, 1889, convalescent.

CASE XVIII.—A. S., female, aged twenty-three, admitted November 4th, 1889. Acutely maniacal; attacks characterised by outbursts of frenzy; destructive, noisy, and using obscene language; at night very restless, noisy, and without sleep; 40 grains of chloralamide had no effect; 50 grains produced only three hours' sleep. On the fourth morning (while using this drug) she was very ill, suffering from emesis; dry brown-coated tongue; no diarrhoea or delirium; temperature 99.2°. Vomiting continued at intervals, for five or six hours. I ceased using this medicine, and have not administered it to her since. She is now much improved mentally.

CASE XIX.—J. B., female, aged fifty-two, admitted July 27th, 1889. A case of melancholia; intensely depressed, with tendency to suicide; replied very little when spoken to; at night was sleepless and very restless; also suffered from chronic bronchitis and weak action of heart. For five consecutive nights she was treated with 30 grain doses of chloralamide, producing sound and refreshing sleep, lasting on an average eight hours. Chloralamide being discontinued, patient continued to sleep well, and is now convalescent.

CASE XX.—O'T., female, aged sixty-five, some years in the asylum. A case of chronic mania. Delusions that things of a dirty nature were in her bed. Immediately the attendant left the dormitory, patient would get out of bed, lie on the floor, and cover herself with the bed-clothing. 25 grains of chloralamide always acted in about half an hour, producing sound and unbroken sleep for seven hours.

In the following cases my colleague, Dr. Nolan, administered, for five to seven consecutive nights, 3iii. elixir of chloralamide (45 grains), with no ill results:—

Initials	Disease	Dose	Average Result, hours of Sleep
J. M., male,	General paralysis of the insane,	45 grains, -	Six hours
J. D., male,	Acute mania, -	45 grains, -	Five hours
H. H., male,	Chronic mania, -	45 grains, -	Five and a half hours
N. R., male,	Acute melancholia, -	45 grains, -	Five and a half hours
A. M., male,	Post-febrile insanity,	45 grains, -	Four and a half hours

I think these cases demonstrate that chloralamide is undoubtedly a sleep-producing agent, that the sleep created varies from five to eight hours, and appears to be sound and refreshing.

A dose of 25 to 35 grains was sufficient to cause sleep in patients suffering from melancholia and chronic mania, but in cases of acute mania small doses had no effect, and sleep was not produced by less than from 40 to 50 grains. No recognised evil effects followed the continued use of this drug for eight days; only one out of twenty-five persons under treatment with chloralamide was noticed to be suffering from gastric disturbances—viz., giddiness and sickness, with dry brown tongue, which followed six hours after a draught, when no sleep ensued (see Case No. XVIII.).

In comparison with other hypnotics, chloralamide, as it consists of a combination of chloral, somewhat resembles it in its action. Both induce sleep, lasting from five to eight hours, but they appear to possess little analgesic influence unless when they cause sleep (see cases Nos. 15 & 16). Unlike opium they will not relieve pain. The time that elapses before sleep is produced varies from thirty minutes to one hour; and the sleep appears to be natural and refreshing. Its action on the circulation is stated to be quite the opposite of that of chloral hydrate, which acts directly upon the

blood pressure, slowing the pulse and respiration, and producing poisonous effects, by direct action on the cardiac ganglia and respiratory centre, causing paralysis of the heart and cessation of respiration. Chloralamide appears, as far as I have been able to ascertain, to be free from such danger. In five cases—one of pneumonia, one of phthisis, one of cardiac disease, and two of insomnia—I obtained sphygmographic tracings before and after its administration, and the blood pressure was not lowered in any of them, while the respiration and temperature remained the same (see cases Nos. 4, 5, 6, 7, 8). Dr. Daniel Leech (*British Medical Journal*, November 2nd, 1889), writing about chloralamide, states that "it seems probable that the formamide element, containing as it does a substitute NH_2 group, will stimulate the circulatory and respiratory centres in the medulla, thus tending to counteract the depressing influence of chloral on them." Reichmann noticed that with doses ranging from 30 to 60 grains the blood pressure was not lowered.

Comparing chloralamide with sulphonal, which has been extensively used in the Richmond District Lunatic Asylum, with very satisfactory results, for the last year and a half, I need not dwell upon the advantages of the latter as a hypnotic agent, because I have practically nothing to add to the observations made by Dr. Conolly Norman (see *Dublin Journal of Medical Science*, January, 1889), and fully confirmed by further experience. Speaking of sulphonal, Dr. Norman states that "its disadvantages are (1) that it is bulky and practically insoluble, therefore difficult to administer, and that, perhaps, owing to its insolubility, (2) it is slow in action," and its price is high. Chloralamide, on the contrary, is not bulky, is tolerably soluble, quick in action (thirty minutes to one hour), and is now cheaper than sulphonal has even yet become.

On the whole it seems that this new hypnotic is well worthy of a trial, having proved for so far safe and reliable.