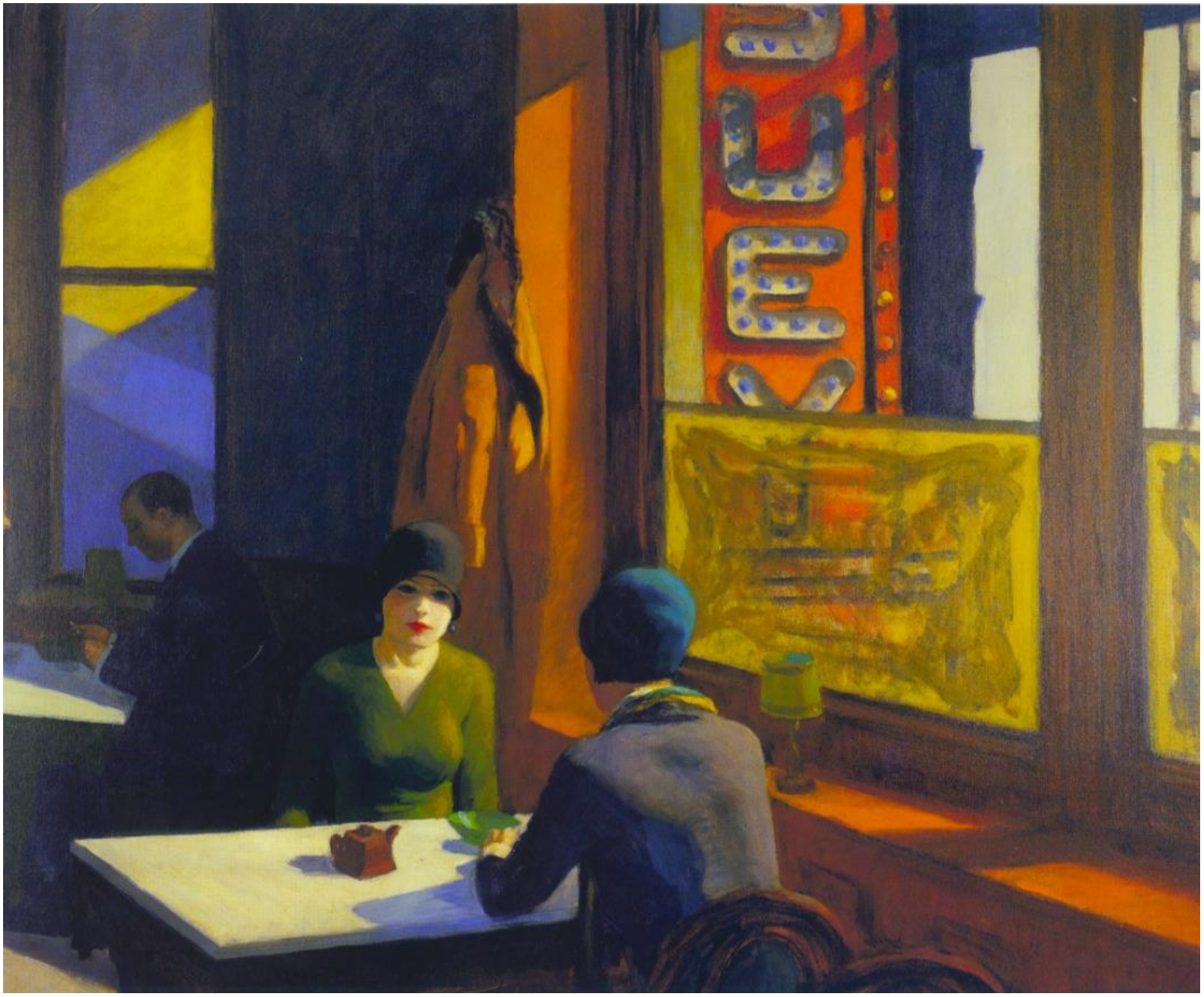
THE NORTHERN HOSPITAL

MOTOR NEURON DISEASE



"Chop Suey", oil on canvas, 1929, Edward Hopper

People were forced into all sorts of tricks and expediencies to survive, all sorts of shabby and humiliating compromises. In thousands and thousands of homes fathers deserted the family and went on the track (became itinerant workers), or perhaps took to drink. Grown sons sat in the kitchen day after day, playing cards, studying the horses (betting on horse racing) and trying to scrounge enough for a threepenny bet, or engaged in petty crime, mothers cohabited with male

boarders who were in work and who might support the family, daughters attempted some amateur prostitution and children were in trouble with the police.

Wendy Lowenstein, Weevils in the Flour: an oral record of the 1930s depression in Australia , Scribe, Melbourne, 1998

2014 - Time Remembers the Great Depression:

When neighbors couldn't get a loan from the bank, they'd come to Dad. He sold farm machinery. He never put his money in a bank. He stored it in a strongbox in the fruit cellar, under the apples. He'd loan the neighbors what they needed and they paid him back when they could. If there was a month - especially the winter months - when they couldn't pay, they'd slaughter a cow or a pig and give him a portion. In the summer it was vegetables: corn, peas, whatever they had growing. The main thing was, Dad never wanted them to lose their land. It was their heritage and how they earned a living. They were farmers. We always lived frugally anyway, so in some ways we didn't know the difference. What you ate in the winter months was what you put away in the summer. The biggest thing that happened is when they decided to pave the dirt road in front of the house. It was the Works Progress Administration (WPA). But my Dad was a Republican, and he was just beside himself.

Gladys Hoffman, age 83

...People really got together. Everybody realized they were in the same boat. If my mother couldn't pay the grocer, he knew that she would the next time there was a paycheck. Everybody was in the spirit of helping out. That's the only thing that saved us.

Robert Hoffman, age 86

I had a very affluent childhood right up until I was about nine. We lived in several gracious homes, I went to a private school, we had a live-in servant and so on. My father had a bulletproof Cadillac he had bought from a bootlegger I was born in New York City because my parents were American citizens and they wanted their children born there. As I always say, my mother came home to foal. My father was a fur trader, though, so I spent most of my childhood in Canada. And then suddenly, our most gracious home was gone. The servants left. I was so dumb that when we were losing the last of our grand houses, I told my classmates that "Gee, bailiffs are coming to our house". I didn't know what a bailiff was or what that meant... I do remember once - my father never quite excused me for saying this - I said to him, "Why don't you become a milk man? Like so-and-so's father, at least he earns $28 a week!" I must have been about 12 or 13 when I said that brilliant thing to my father!

Judith Crist age 86, she worked for over 30 years as a reporter and film critic at the New York Herald Tribune, TV Guide and New York Magazine.

I was born in 1928 in Carmine, Illinois, where I live now. We raised watermelons and corn and you just couldn't sell anything. Nobody was buying any of our commodities. I remember we loaded them on train cars and sent them to Chicago to the market. And I can remember we sent them up there with the idea that they'd send us some money back. Well, the sellers went broke and didn't send us the money. And then we got a call from the railroad company wanting us to pay the freight (Laughs). Back in those days, we didn't have anything to speak of – didn't have electricity, didn't have indoor plumbing. We didn't even have a radio. I remember my mother

wanting a telephone, and dad didn't think we could afford it. They had a heck of an argument over it. It was rough, but everybody was in the same boat. Nobody had anything. Every room had a stove then, we didn't have furnaces, you know. And a lot of people didn't have wood and couldn't afford coal. People were actually burning their corn for heat. You couldn't sell it, so might as well do something with it. We came home one night and somebody had broken into our house and stolen all our food. They didn't want money, they just had to have food. We had livestock so we always had meat. We were pretty self-sufficient in that way. The people who were really hurting, I think, were the people who worked in the cities.

Lance Brown age 80

Oh gosh, where to start. I was born and raised in Boston, born in 1930. I am an only child. My mother died when I was 5. My father was an immigrant from Ireland and extremely intelligent and politically active. He was a headwaiter at that time in some of the most exclusive clubs in Boston. He believed in taking me to downtown Boston during the Depression and showing me the devastation. He took me down to Boylston Street, down around Boston Common and showed me the people who were sleeping on the ground, who had nothing to eat, with holes in their shoes, standing on the corner, peddling apples. He explained to me what was happening and obviously it left an impression because I still remember it…

Patricia Johnson, age 78

In 1932, we lived in a two-family house in Flatbush, Brooklyn. I remember seeing well-dressed men on bread lines, selling apples on the corner of Canal and Broadway in Manhattan, near where my father had a factory. He owned a chemical company, and had to let his employees go - both the workers and the salesmen… It scarred me for life. It made me very conservative in my spending.

Rhoda Fidler age 86

Mother at least had a salary for nine months of the year. And that was good. We didn't have any money at all, but she scraped by. She always said one of the great things about the Depression was how the people came together…

Henry Hager age 82

My family settled in Richmond, Virginia in 1928 and when the crash came a year later it wiped out pretty much all of the investments my father had. My father was totally deaf as a result of having diphtheria when he was a boy, and was unequipped to hold the average kind of job. I remember that in the summer of 1932 when my father was really strapped for money, he decided he needed a trade to practice and somehow learned to make sweeping brooms, figuring that people use them everywhere and they wear out. I remember walking from my home with my brother about a mile up the street to where my father had rented a small, square concrete building that was totally bare except he had managed to put a broom-making machine in it. He had stacks of broom straw, wire, wood, and the machine. My father said he was gonna take us two boys out to try to sell some brooms. We piled into the car and drove from country store to country store, watching as my father peddled brooms at some places and got turned away at others. I remember he told my mother one time if he could make 50 cents a day he would be OK…

Rev. Edward Morgan III, 83

We had another family that lived on the farm during that time and the father had to go to the soup line, that's what we called it. And he got flour and lard and powdered milk and powdered eggs for his family to live on. They just didn't have anything.

Owen Hasset, age 89

I remember my father and grandparents trying so hard to save our ranch. The bank failed and new managers came in. They didn't know anything about farming and they wouldn't loan money. Our cattle were auctioned off by the bank. At the auction, some of our neighbors bought my pony and gave it back to us. They saved a cow for us that way. My mother would take her crate of eggs into the stores and she would bargain with them and that's how we got our food and our clothing. I remember the morning grandmother went to her linen closet and took out a cigar box where she kept her chicken money. She counted it and parceled it out to my father and his brother and kept some for herself just to have grocery money. My family were stoic Scots. You didn't see them cry and carry on. But I remember so vividly when we got ready to go home, grandma just tousled my hair and said, "Thank you for coming with your daddy. This has been a hard day".

Ernestine McMillan Hilton, 88

In 1929 the Wall Street Stock Market crashed, with exponentially cascading catastrophic effects for the industrialized nations of the Western world. Not before or since has such a disastrous economic event gripped the modern "first world" on such a global scale. Unemployment rates in Europe, North America and Australia soared to well over 30 %. The generation that lived through the event were scarred for life. They developed a sense of frugality - and a touching appreciative thanks for whatever small material comforts in life they did have. The times were recorded for posterity in a new Art genre that came to be known as "Social Realism" - stark depictions of everyday reality. Gone were the traditional depictions of the "noble peasant" - there was nothing noble in the sad images of those living on the breadline in the cities. The genre is best exemplified by the haunting works of Edward Hopper. Lonely people in lonely cities - dreamlike images devoid of all unnecessary surrounding objects one would find in real life - as if to emphasize a lack of material possessions - unimaginable to the current generation - just desperate people eating in the very cheapest of restaurants because they had no gas or electricity at home - their "meals" a mere cup of tea or a simple bowl of chop suey. Many could not even afford these, but rather merely gathered together in a sense of common adversity, for support and companionship.

A diagnosis of motor neuron disease is a catastrophic one for those who receive it. The disease in invariably fatal, and there is no current cure. As in an Edward Hopper image we see that the very soul is destroyed, as all hope is gone. In these circumstances support and comfort is of critical importance - even of the simplest nature.

MOTOR NEURON DISEASE

Introduction

Motor neuron disease is a catastrophic neurodegenerative disease of the motor neuron system.

It is a progressive neuromuscular disorder of the upper and lower motor neurons resulting in limb, bulbar and respiratory muscle paralysis.

It is one of the most feared diagnoses in modern medicine because of its universally fatal outcome.

Its aetiology is unknown.

Amyotrophic lateral sclerosis (ALS) is the most common form of motor neuron disease. The disorder is named for its underlying pathophysiological processes:

- "Amyotrophy":
  - ♥ This refers to the atrophy of muscle fibers, which become denervated as their corresponding **anterior horn** cells degenerate.
- "Lateral sclerosis":
  - ♥ This refers to the changes seen in the lateral columns of the spinal cord as upper motor neuron (UMN) axons in these areas degenerate and are replaced by fibrous astrocytes (gliosis).

Amyotrophic lateral sclerosis is incurable and fatal, with a median survival time from the onset of weakness of just 3 years.

Treatment is predominantly supportive and aims to extend the length of life as well as the meaningful quality of life for patients.

Medical treatments are very limited in what can be achieved. Allied health disciplines become vitally important in the management of patients with motor neuron disease.

ED presentations will predominantly relate to:

- **Aspiration pneumonia**
- **The secondary complications of increasing immobility**
- **Social crises - inability to cope with requirements of normal living.**
- **Depression and attempted suicide**

- **End of life care**

History

ALS was first described in **1869** by the French neurologist **Jean-Martin Charcot** and for a while became known as **Charcot disease.**

In 1939 ALS became popularly known as **Lou Gehrig** disease, after a baseball player by that name, contracted the disease in 1939.

Epidemiology

The mean age of onset of sporadic ALS is 65 years.

The mean age of onset of familial ALS ranges from 46-55 years

Pathophysiology

Pathology:

The aetiology of ALS is unknown.

ALS should probably not be considered a single disease entity, but rather a clinical diagnosis for different pathophysiologic cascades that share the common final consequence of resulting in preferential progressive loss of motor neurons.

Some cases may have a **genetic predisposition.** A family history of the disease is obtained in about 5 % of patients, and twin studies have shown a genetic contribution with heritability of about 60 %.

In some cases, ALS overlaps clinically, pathologically, and biologically with **frontotemporal dementia**, and it may share common biologic mechanisms with Alzheimer disease, Parkinson disease, and other neurodegenerative diseases.

Cigarette smoking is the only exogenous risk factor that is thought to be a risk factor for the development of ALS.

Complications:

These include:

1. Aspiration pneumonia (frequent as bulbar palsy progresses)

2. Progressive ventilatory failure:

    - The most common cause of death.

3. The medical complications of increasing immobility, including:

- Stasis pneumonia
- GIT ileus
- UTI
- Venous thromboembolic disease: DVT and PE.
- Pressure ulceration and necrosis.

4. Progressive inability to perform the normal activities of daily living (ADLs).

5. Depression:

   - Profound depression with suicidal ideation are very commonly seen.

Clinical Features

Clinical variants

The 4 main clinical types of motor neuron disease are:

1. Classic ALS (Upper and lower motor neurons):

   - The term classic ALS is reserved for the form of disease that involves **upper and lower motor neurons.**
   - The classic form of sporadic ALS usually starts as dysfunction or weakness in one part of the body and spreads gradually within that part and then to the rest of the body.
   - Ventilatory failure results in death 3 years, on average, after the onset of focal weakness.
   - The rate of disease progression varies widely, however, with some patients dying a few months after experiencing their first symptom and others still walking 10 years afterward.

2. Progressive muscular atrophy and flail limb syndrome (LMNs) :

   - The disease may be restricted to **LMNs.**
   - When the pattern of LMN involvement is asymmetrical, the disorder is termed **progressive muscular atrophy (PMA),** and the course is usually indistinguishable from that of classic ALS.

- Patients with a symmetrical pattern, called flail limb syndrome, have a course that may be far longer.

3. Primary lateral sclerosis (UMNs):

- When only **UMNs** are involved, the disease is called **primary lateral sclerosis (PLS)**.

- The course of PLS differs from that of ALS and is usually measured in decades.

4. Progressive bulbar palsy (Isolated bulbar involvement):

- Rarely, the disease is restricted to bulbar muscles, in which case it is called **progressive bulbar palsy (PBP).**

- In most patients who present with initial involvement of bulbar muscles, the disease eventually evolves to classic ALS.

Classical presenting clinical features:

In 75 - 80 % of patients, symptoms begin with **limb** involvement.

About 20 % begin with **bulbar** involvement.

For those with limb involvement at presentation, the frequency of upper limb versus lower limb involvement is approximately equal.

Initial complaints in patients with **lower limb onset** include:

- Tripping, stumbling, or awkwardness when running.

- Foot drop; patients may report a “slapping” gait.

Initial complaints with **upper limb** onset include:

- Reduced finger dexterity, cramping, stiffness, and weakness or wasting of intrinsic hand muscles

- Wrist drop interfering with work performance

Initial complaints in patients with **bulbar onset** include:

- Slurred speech, hoarseness, or decreased volume of speech

- Aspiration or choking during a meal

Emotional and special cognitive difficulties in some ALS patients are the result of the loss of prefrontal neurons. Clinical manifestations may include:

- Emotionally lability
- Depression.
- Impaired executive functions
- Maladaptive social behaviors

Features of **more-advanced** disease include:

- Muscle atrophy
- Spasticity compromising gait and manual dexterity
- Muscle cramps
- Rarely, painful joint contractures may result from immobility

Progression of **bulbar disease** leads to:

- Voice changes:
    - ♥ Hypernasality and development of a strained, strangled vocal quality; eventually, speech may be lost completely.
- Swallowing difficulties:
    - ♥ Usually starting with liquids
- Drooling/ inability to swallow saliva.

Making the Diagnosis:

Definitive diagnosis may not be possible with **early** ALS.

Confirmation of the disease may require a period of observation to document its **progressive nature** and to **exclude alternative diagnoses.**

The World Federation of Neurology (WFN) has developed a diagnostic algorithm that combines the clinical and, in some cases, electrophysiological findings.

The degree of certainty of diagnosis is increased by the number of body segments that demonstrate upper motor neuron (UMN) and lower motor neuron (LMN) signs.

UMN signs are:

- Mild weakness
- Spasticity
- Abnormally brisk reflexes.
- Presence of abnormal reflexes (e.g., Babinski, Chaddock, or Hoffman signs)

LMN signs are:

- Progressive flaccid weakness
- Wasting
- Fasciculations:
    - ♥ Particularly in the tongue and limbs.
- Loss of reflexes
- Loss of muscle tone.

Bulbar symptoms:

These predominantly manifest as:

- Dysarthria
- Dysphagia
- Impaired cough reflex.
- Impaired gag reflex

The WFN criteria recognize the following 4 regions, or levels, (or segments) of the body when describing the symptoms of motor neuron disease:

- Bulbar:
    - ♥ Muscles of the face, mouth, and throat
- Cervical:
    - ♥ Muscles of the back of the head and the neck, shoulders, upper back, and upper extremities

- Thoracic:
    - ♥ Muscles of the chest and abdomen and the middle portion of the spinal muscles
- Lumbosacral:
    - ♥ Muscles of the lower back, groin, and lower extremities

The current WFN categories of diagnosis are as follows:

Clinically definite ALS:

- UMN and LMN signs in at least 3 body segments

Clinically probable:

- ALS: UMN and LMN signs in at least 2 body segments with some UMN signs in a segment above the LMN signs.

Clinically probable, laboratory supported ALS:

- UMN and LMN signs in 1 segment or UMN signs in 1 region coupled with LMN signs by electromyography (EMG) in at least 2 limbs.

Clinically possible ALS:

- UMN and LMN signs in 1 body segment, UMN signs alone in at least 2 segments, or LMN signs in segments above UMN signs.

Clinically suspected ALS:

- Pure LMN syndrome with other causes of LMN disease adequately excluded.

Investigations

Electromyography (EMG):

The diagnosis of ALS is primarily clinical, but electrodiagnostic testing can contribute to the diagnostic accuracy.

The hallmark EMG findings of ALS are:

- Normal sensory nerve conduction studies.

And

- Abnormal motor nerve conduction studies, (with reduced motor compound muscle action potentials).

The needle exam shows changes characteristic of ongoing denervation and re-innervation of muscles.

Genetic testing:

In patients with **familial** ALS, genetic testing may be done after appropriate counselling.

Tests for the SOD1, TARDBP (coding for TDP- 43), FUS, ANG, C9orf72, and FIG4 genes and for the gene causing Kennedy disease are generally available.

Patients with other forms of familial ALS may be referred to centres with a specific research interest in familial ALS.

Muscle and/ or nerve biopsy:

Muscle or nerve biopsy is not usually required, but may be considered if the presentation of ALS is atypical.

MRI scanning:

This is sued primarily to rule out alternative diagnoses, such as multiple sclerosis or structural lesions.

PET Scanning:

The value of positron emission tomography (PET) scanning is under investigation.

Management

ED presentations will predominantly relate to:

- **Aspiration pneumonia**
- **The secondary complications of increasing immobility**
- **Social crises - inability to cope**
- **Depression and attempted suicide**
- **End of life care**

In general terms treatment consists of:

Pharmacological treatments:

1. **Riluzole:** [2]

There is **no** curative treatment currently available.

The glutamate antagonist riluzole is the only medication that has shown (marginal) efficacy in ALS.

- Riluzole may result in modest slowing of disease progression.

  The median extension of life by riluzole in placebo-controlled studies was 2-3 months

  Use:

  Riluzole 50 mg orally, twice daily.

  Patients on riluzole should have their liver biochemistry and full blood count checked monthly for the first 6 months. Hepatic disturbance and neutropenia are uncommon adverse effects.

2. Baclofen: [2]

Muscle cramps are common and may be helped by baclofen

- Give 10 mg orally, twice daily
- It should be kept in mind that baclofen is potentially lethal when taken as a deliberate overdose.

See separate document of Baclofen overdose.

3. NSAIDs: [2]

- Myalgias may respond to short courses of non-steroidal anti-inflammatory drugs.

4. Antidepressants/ antianxiety agents:

- These are important for most patients an should be prescribed as required.
- When prescribing these agents it is important to consider the toxicity of each agent if taken in acute intentional overdose. This risk should be balanced against the patient's needs on a case by case basis.

5. Glycopyrrolate:

- This agent is useful for drying distressing secretions, especially in situations of end of life care

Medications which reduce respiratory drive, such as opioids, should be avoided or at least minimized as far a possible.

Ventilatory support:

The early use of noninvasive ventilation (NIV) especially nocturnally prolongs survival.

It also improves the quality of life.

NIV should be considered at the earliest sign of nocturnal hypoventilation or respiratory insufficiency.

Mechanical insufflation/exsufflation may be considered to clear secretions in patients with reduced peak cough flow, particularly during an acute lower respiratory infections

Some patients want to be kept alive using long-term invasive ventilatory support.

Feeding gastrostomy:

Enteral nutrition via percutaneous endoscopic gastrostomy (PEG tube) can somewhat prolong life, however this treatment must be balanced against overall quality of life.

This treatment is very much an "end-game" strategy and will be heavily dependent on the patient's own wishes as well as family support.

Speech pathology:

- The speech pathologist is an essential member of the management team for patients with motor neuron disease.

  In particular they can assess the ability of patients to swallow food and fluids, a vital aspect of assessing patients who present to the ED with problems related to feeding and/ or aspiration

Psychological support:

- Depression and anxiety are a major feature of motor neuron disease and intense psychological and/ or psychiatric support is vital.

Social work

- With increasing severity of illness, social factors including the ability to cope in the community become increasingly important.

Occupational therapy

- With increasing severity of illness, social factors including the ability to ADLs will become increasingly compromised.

Physiotherapy

- Physiotherapy may also be appropriate depending on the nature of the patient's symptoms.

Alternative therapies:

Many patients with ALS turn to "alternative therapies" in desperation.

If not unsafe or extortionately priced, these "treatments" may be a reasonable way of giving some patients a sense of some control, and a feeling of physiological comfort, and these needs should not be ignored

Since most, if not all, alternative therapies have not been tested against placebo controls, physicians cannot provide blanket recommendations for their use.

When alternative therapies impose a great burden on patients, in terms of cost and/or time commitments, or to the detriment of proven medical treatments they should be discouraged.

End-of-life considerations:

End-of-life issues should ideally be discussed and clarified early.

However, this may not work well for some patients.

The physician should be aware of the individual state or national laws that regulate these issues; encourage, if appropriate for the patient, completion of advance care directives; and document the patient's preferences in the medical records, (whether or not formal advance directives have been written).

Clinical trials

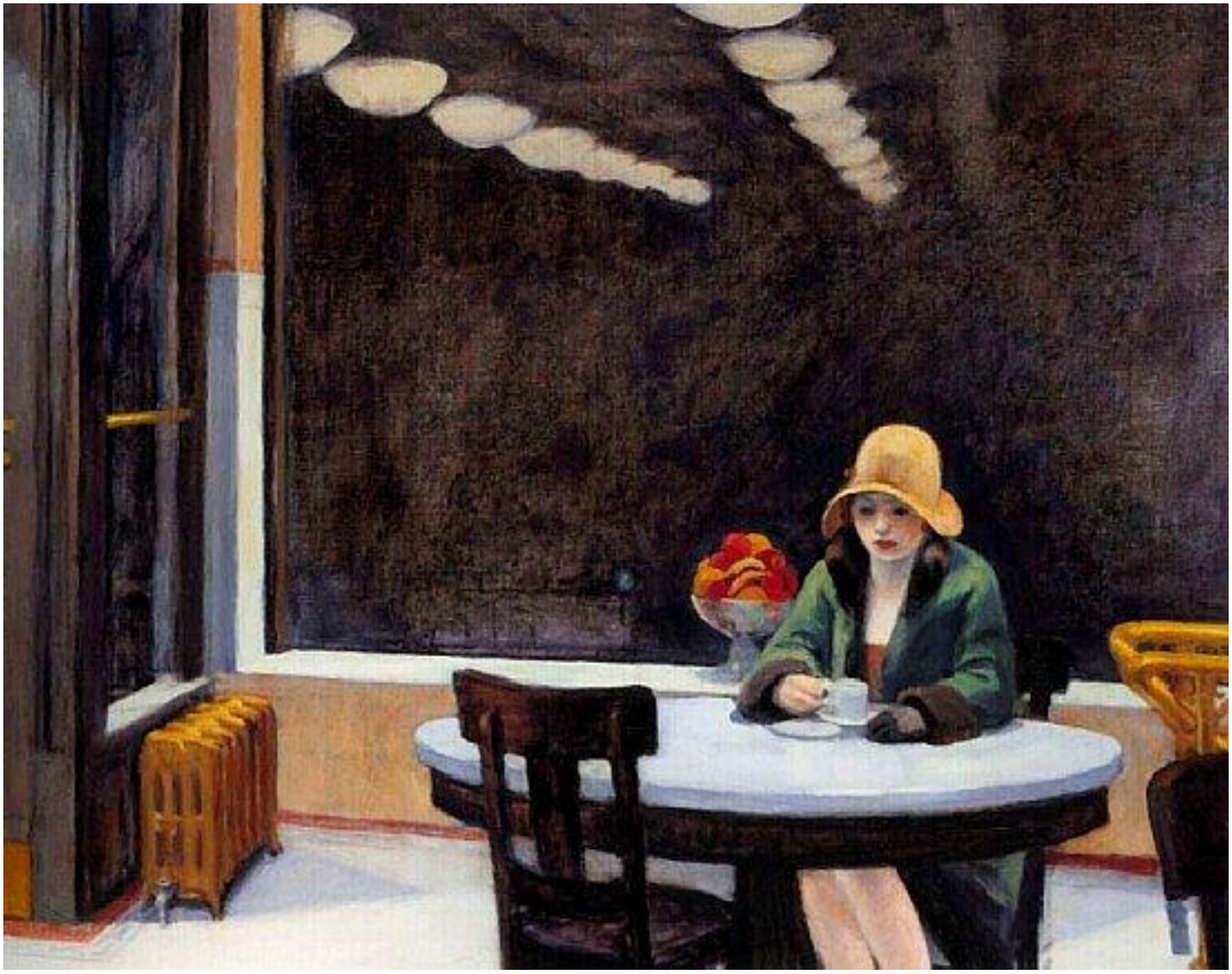
Some patients with ALS may wish to help with the search for treatments for the disease through participation in clinical trials

Patient Resources

In an era of readily available information on the Internet, provision of the diagnosis will generate independent activity on the part of patients, families and friends to educate themselves about the disease.

Thus, it is helpful if clinicians point patients and the families to those resources that they feel will serve this purpose best, to at least serve as a starting point.

Support groups are available to patients in many communities. Burnout of the primary caregiver needs to be anticipated and avoided by assuring that the primary caregiver is not the only caregiver.



"Automat", oil on canvas, 1927, Edward Hopper.

One of the most poignant of Hopper's works of Social Realism was actually painted two years before the Wall Street collapse. After this event his works took on a mass popular appeal. Ordinary people identified with his works far more closely. His famous "Chop Suey" followed after the crash in 1929. He continued in this genre well into the 1940s, when he produced his most famous work - the iconic "Nighthawks", which now hangs in The Art Institute of Chicago, (see Document on Loneliness - Social Emergencies folder).

"The Bread Line", bronze, George Segal, 1997, Franklin Delano Roosevelt Memorial, Washington, DC

Segal's bronze, is a more modern work of the genre of "Social Realism", that thrived in the 1930s and early 1940s. It is part of the memorial to Franklin Delano Roosevelt, in Washington DC. Social Realism was primarily an America phenomenon, that made statements about the desperate economic conditions of that decade - but the genre did gain adherents in Europe after the Second World War who painted working class interiors and still-lives that made social commentary on the effects of that terrible conflict on people's lives.

*In the USSR, aspects of Social Realism also became popular among artists, but in the repressive regime of the Bolsheviks it was commandeered by them and very quickly became highly politicized. So although making realistic (as opposed to abstract) depictions of everyday life its message in contrast to the West's was one of optimism - promoting the heroic struggle of the poor in their efforts to support the Revolution. Because of this heavy political control, the genre in the Soviet Union became known as "**Socialist** Realism". In 1934 Joseph Stalin made Socialist Realism the official state sponsored Art, replacing Constructivism - no other form of Art would be allowed until the collapse of the Soviet Union in 1991.*

References

1. Amyotrophic lateral sclerosis in eMedicine Website,

2. eTG - July 2014:

    - Neurology Therapeutic Guidelines, 4th ed 2011.

Dr J. Hayes
October 2014